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This Position Document addresses the risks and benefits of pesticide products containing the subject active ingredient. The Agency has determined that the use of products containing the subject active ingredient may meet or exceed a risk criterion described in 40 CFR Part 154. Potential hazards will be examined further to determine the nature and extent of the risk, and considering the benefits of the subject active ingredient, whether such risks cause unreasonable adverse effects on the environment.

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CYANAZINE

SPECIAL REVIEW

TECHNICAL SUPPORT DOCUMENT

Office of Pesticide Programs
Office of Pesticides and Toxic Substances
United States Environmental Protection Agency
401 M Street, SW.
Washington, DC 20460

December 29, 1986

EXECUTIVE SUMMARY

In April 1985, EPA issued a Notice of Special Review (also called Position Document 1 or "PD 1") on pesticide products containing cyanazine (50 FR 14151). The Special Review was based on teratology studies using oral administration which showed that cyanazine produces teratogenic effects in the Fischer 344 rat (25 mg/kg, NOEL = 10 mg/kg) and fetotoxic effects in the New Zealand white rabbit (2 mg/kg, NOEL = 1 mg/kg); the risk criterion listed in 40 CFR section 162.11 was exceeded. Exposure to mixers/loaders and applicators were identified as the occupational exposures of concern. For the unprotected agricultural worker, the risk assessments presented in the cyanazine Registration Standard and PD 1 gave doses which were likely to be close or comparable to the levels where effects occurred in laboratory animals.

The cyanazine Special Review also stated that cyanazine has been found in ground water and surface water. Monitoring data have been required from the registrant. All data are due to be submitted to the Agency by January 1987. A decision on whether to initiate a Special Review based on risks resulting from ground water contamination will be made after the data are submitted and reviewed.

Cyanazine is the accepted, common name for 2-[4-chloro-6-(ethylamino)-s-triazine-2-yl]amino]-2-methylpropionitrile, and its trade name is Bladex®. Cyanazine is a pre- or post-emergent herbicide, registered for use to control annual grasses and broadleaf weeds in corn, cotton, grain sorghum (milo), and fallow cropland which may subsequently be planted to wheat. Approximately 95% of the total domestic usage is on corn. Cotton (3%) is the second most common use, and grain sorghum (1%) and wheat fallow (<1%) are the other use sites.

As part of the Special Review process, the Agency evaluates the risks and benefits associated with the uses of a pesticide. Where appropriate, regulatory actions are proposed which are necessary to ensure that the continued use of the pesticide does not result in unreasonable adverse effects.

Dermal absorption and dermal developmental toxicity studies have been submitted to the Agency since the issuance of the Notice of Special Review on cyanazine. These data have refined the risk estimates, and risk assessments on non-dietary exposure to cyanazine have been completed. They are based, in part, on an exposure study submitted by one of the registrants and on the newly submitted dermal developmental toxicity study in New Zealand rabbits. This study demonstrated a no-observable-effect-level (NOEL) of 573 mg/kg/day.

Regarding benefits, growers select cyanazine over currently available herbicides for the following reasons: 1) it has a wide annual broadleaf and grass weed control spectrum; 2) it can be tank mixed with a number of herbicides to broaden its weed control spectrum; 3) it has relatively short persistence in the soil; and 4) it has no rotational crop restrictions.

The degree of risk varies, depending on the use rate and the number of acres treated. Approximately 99% of cyanazine use is applied by ground boom application. The Agency has determined that the risks (margins-of-safety) are unacceptable for all application rates to corn, cotton, grain sorghum, and wheat fallow during ground boom application unless protective gloves are worn for mixing and loading operations and when adjusting, repairing, or cleaning equipment. Less than 1% of cyanazine use is applied aerially or by chemigation. The Agency has determined that the risks (margins-of-safety) to mixer/loaders during aerial use or chemigation are not acceptable unless protective gloves are worn during mixing and loading operations and when adjusting, repairing, or cleaning equipment and a closed loading system is used.

The Agency is proposing that cyanazine labels require the use of protective gloves when mixing or loading or when adjusting, repairing or cleaning equipment during or following ground boom application; however, even with the use of protective gloves, the risks may not be acceptable when accidental spills occur or if a person leans against the mixing tank. Therefore, the Agency is proposing that labels require a chemical resistant apron to be worn during mixing and/or loading operations for ground boom application.

As noted, the Agency has determined that current cyanazine labels are not adequate to reduce risks posed by aerial use or chemigation. The Agency is proposing that cyanazine labels require the use of protective gloves for mixing and and loading operations and when adjusting, repairing, or cleaning equipment, and the use of closed loading systems when cyanazine is to be applied through aerial or chemigation methods. Furthermore, due to the potential risks posed by possible ruptured hoses and other closed system failures or by exposure to the body from leaning against mixing tanks, the Agency is also proposing that labels require the use of a chemical resistant apron when mixing and/or loading cyanazine as part of aerial use or chemigation. In addition, some cyanazine formulations (wettable powders and granulars) are not physically compatible for use with closed loading systems; therefore, the Agency is proposing that aerial use and chemigation be prohibited on the labels of these formulations.

2

Exposure studies using other pesticides were used to estimate exposure to cyanazine through spray drift. Based on these exposure estimates the risk for a population exposed to cyanazine by spray drift appears to be acceptable. In addition, secondary exposure may also occur when clothing worn during cyanazine use is handled or when contaminated clothes are brought home and laundered with household laundry. Therefore, the Agency is proposing that language be added to all cyanazine labels regarding the proper laundering and disposal of cyanazine contaminated clothes. Furthermore, because hands receive the largest percentage of the dermal exposure during mixing/loading, it can be assumed that when protective gloves are worn, these gloves will be contaminated on the outside with a large percentage of the cyanazine being handled. Therefore, the Agency is proposing that language be added to all cyanazine labels which states that protective gloves should be washed with soap and water after use and before being removed from the hands.

All cyanazine products are already required to be classified for restricted use. Furthermore, Agency policy states that when a pesticide is classified for restricted use, the reason for that classification must be printed in the "Restricted Use" statement which appears on the label. Therefore, all cyanazine labels are required to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water.

Risk assessments for dietary exposure did not indicate that a Special Review criterion had been met for this route of exposure. However, additional data to determine the residue levels of metabolites have been required. (Cyanazine is a triazine herbicide, and the metabolites of concern include the chloro- and hydroxytriazine metabolites.) A combined tolerance for cyanazine and its metabolites will be determined after such metabolite data are reviewed. The risk assessments for dietary exposure will be re-examined after combined residues of cyanazine and its metabolites have been quantified.

The label changes mentioned above and discussed in this Technical Support Document are in addition to those put forth in the cyanazine Registration Standard; EPA issued the Registration Standard for pesticide products containing cyanazine in December 1984. In addition to requiring that certain data be submitted, the Registration Standard announced the Agency's position on continued registration, including label changes which must be made. Among these required changes were additional statements regarding: cyanazine being made a restricted use pesticide; ground water contamination resulting from agricultural use of cyanazine; and cyanazine being the cause of birth defects in laboratory animals.

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TABLE OF CONTENTS

Page

Executive Summary i
Acknowledgements iv

I. INTRODUCTION

A. General Background and Organization I-1

B. Legal Background I-2

C. Regulatory History of Cyanazine

1. Uses and Registration I-3

2. Tolerances I-7

3. Interim Risk Reduction Measures I-8

II. ASSESSMENT OF RISKS AND ANALYSIS OF PUBLIC COMMENTS

A. Basis of Presumption II-1

B. Hazard Identification

1. Physical - Chemical Properties and Exposure Pathways II-1

2. Structure - Activity Relationships II-1

3. Teratogenicity II-3

4. Weight-of-the-Evidence II-5

C. Dose-Response Assessment II-5

D. Exposure Assessment - Non-dietary Exposure to Cyanazine

1. Ground Boom Application to Field Crops . . . II-6

2. Aerial Application to Crops II-13

3. Chemigation II-15

E. Risk Characterization - Non-Dietary Risks . . . II-17

TABLE OF CONTENTS (continued)

F. Other Possible Exposure Concerns
   1. Dietary II-19
   2. Ground water and Surface Water II-21
   3. Spray Drift II-22
   4. Secondary Exposure II-22
G. Analysis of Rebuttal Comment Concerning Teratogenic Effects II-23
H. Analyses of Rebuttal Comments Concerning Exposure . II-24

III. BENEFITS SUMMARY
A. Introduction III-1
B. Ground Boom Application III-1
   1. Corn III-1
   2. Wheat Fallow III-4
   3. Cotton III-6
   4. Grain Sorghum III-6
C. Cyanazine Application Via Chemigation III-7
D. Cyanazine Application Via Aerial Equipment III-7
E. Analysis of Rebuttal Comments Concerning Benefits . III-8

IV. REGULATORY OPTIONS AND RISK/BENEFIT ANALYSIS
A. Introduction IV-1
B. Risk Conclusions IV-1
C. Benefit Conclusions IV-2
D. Development of Regulatory Options IV-3
   1. Ground Boom Application IV-3
   2. Aerial Application and Chemigation IV-4
   3. Secondary Exposure IV-4
E. Summary of Proposed Decision IV-4
F. Procedural Matters IV-5

V. BIBLIOGRAPHY V-1

I. INTRODUCTION

A. General Background and Organization

On April 10, 1985, EPA issued a Notice of Special Review (also called Position Document 1 or "PD 1") for pesticide products containing cyanazine (50 FR 14151). EPA initiated the Special Review following the determination that cyanazine met or exceeded the risk criterion in 40 CFR 162.11 (a)(3)(ii)(B). That section provides that a Special Review (previously known as a Rebuttable Presumption Against Registration or "RPAR") shall be conducted if the use of a pesticide "[p]roduces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety* . . ." The Special Review was based on studies showing that cyanazine was teratogenic and fetotoxic in laboratory animals. Specifically, a supplementary study (Shell 1981) with Fisher 344 rats showed cyanazine to be teratogenic at 25 mg/kg. The teratogenic effects were anophthalmia (no eyes), microphthalmia (small eyes), and diaphragmatic hernia. Cyanazine also caused fetotoxic effects when fed to rabbits (Shell 1982) at 2 mg/kg, with dilated brain ventricles, anophthalmia, and microphthalmia at 4 mg/kg. The developmental toxicity no-observed-effect-level (NOEL) for this study was 1 mg/kg. The Agency determined that a significant risk was posed through dermal exposure to mixer/loaders and applicators who use pesticide products containing cyanazine.

The basis of EPA's decision to initiate the Special Review on cyanazine is further detailed in a document entitled "Guidance for the Reregistration of Pesticide Products Containing Cyanazine" (Guidance Document) which was issued in December 1984. In the PD 1, which was issued in April 1985, EPA solicited comments on the risks and benefits associated with all uses of cyanazine.

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* The new, revised risk criterion for chronic or delayed toxic effects, issued in the November 27, 1985 FEDERAL REGISTER, incorporates oncogenic, heritable genetic, teratogenic, fetotoxic, or reproductive effects, as well as other chronic or delayed toxic effects. [See 40 CFR 154.7(a)(2).]

After the Special Review was initiated on cyanazine, Shell submitted a dermal absorption study and two dermal teratology studies. The dermal absorption study was classified as Core Minimum (i.e. the study was found to be acceptable and valid for quantitative risk assessment) and demonstrated that dermal absorption of ^{14}C-Bladex in rats over 8 days was 2% of the applied dose. The first dermal teratology study which was submitted was classified as Supplementary Data (i.e. the study was found to provide information, but because the number of litters per group was insufficient and because a NOEL could not be established for this study, the study was not used for quantitative risk assessment). This dermal developmental toxicity study was in New Zealand rabbits using the Bladex 4L formulation and resulted in maternal toxicity at all dose levels, including the lowest dose used; therefore, a NOEL for maternal toxicity could not be established for this study, and the lowest-effect-level (LEL) was established at the lowest dose used, 0.2 ml/kg. The second dermal teratology study was a repeat study. In this repeat study, a maternal NOEL was demonstrated at < 96 mg/kg (lowest dose tested), and the developmental toxicity NOEL was established at 573 mg/kg.

The potential adverse effects associated with the use of cyanazine have been examined further to determine their extent and whether, in light of the benefits of cyanazine, such risks were "unreasonable." This Technical Support Document addresses the risks and benefits of cyanazine use and is comprised of four parts. Part I is this introductory section. Part II evaluates the potential risks associated with cyanazine use, including: analyses of rebuttal comments regarding risk from cyanazine use which were submitted in response to the cyanazine PD 1; descriptions and evaluations of the risk evidence; exposure data; and the Agency's risk assessments. Part III estimates and summarizes the economic benefits associated with cyanazine use and presents analyses of public comments related to benefits. Part IV discusses the development of regulatory options, including the regulatory options considered to reduce the risks and the regulatory actions proposed by the Agency.

B. Legal Background

1. The Statute

A pesticide product may be sold or distributed in the United States only if it is registered or exempt from registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended (7 U.S.C. 136 et seq.). Before a product can be registered it must be shown that it can be used without "unreasonable adverse effects on the environment" (FIFRA section 3(c)(5)), that is, without causing "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of the pesticide" (FIFRA section 2(bb)). The burden of proving that a pesticide meets this standard for registration is, at all times, on the proponent of initial or continued registration. If at any time the Agency determines that a pesticide no longer meets this standard for registration, then the Administrator may cancel this registration under section 6 of FIFRA.

2. The Special Review Process

The Special Review process, formerly called the Rebuttable Presumption Against Registration (RPAR), is a mechanism by which the Agency collects information on the risks and benefits associated with the uses of pesticides to determine whether any use causes unreasonable adverse effects to human health or the environment. The Special Review process is currently governed by 40 CFR Part 154.

Through the Special Review process the Agency (1) announces and describes the Agency's finding that use of a pesticide meets one or more of the risk criteria; (2) establishes a public docket; (3) solicits comments from the public and, under certain circumstances, from the Secretary of Agriculture and the Scientific Advisory Panel regarding the Agency's analysis and proposed regulatory decisions; (4) reviews and responds to all significant comments submitted in a timely manner; and (5) makes a final regulatory decision based on a balancing of risks and benefits associated with a pesticide's use.

C. Regulatory History of Cyanazine

1. Uses and Registration

Cyanazine was registered in 1971 by the Shell Chemical Company under the trade name, Bladex®. Cyanazine has been registered for use in the United States by the Shell Chemical Company, Setre, Inc., and R.F. Lindsey and Sons. Cyanazine is a pre- or postemergent, triazine herbicide which is registered for use to control annual grasses and broadleaf weeds, both before and shortly after they emerge from the soil. Cyanazine is registered for use on corn, cotton, grain sorghum (milo), and wheat fallow. Approximately 95 percent of the total domestic use is on corn. Cotton (3%) is the second most common site, and grain sorghum (1%) and wheat fallow (<1%) are the least common sites. The total usage of cyanazine in the United States is estimated to be at 22 to 24 million pounds of the active ingredient per year.

Application rates of the single active ingredient range from 0.6 to 6 lb active ingredient per acre. Single active ingredient formulations include an 80% wettable powder, 10% and 15% granular forms, a 90% dry flowable form, and a 4 lb/gal flowable concentrate. As currently registered, these formulations may be applied with either ground or aerial equipment. They may also be applied by chemigation with the exception of the wettable powder formulation. To activate the herbicide, one and one-half to two inches of moisture (rainfall or irrigation) are required within 10 days of application. If such moisture is not available within the 10-day period, a shallow incorporation is recommended on labels, with the specific type of equipment and method of incorporation determined by site and equipment availability.

When applied preemergence, cyanazine is applied before, at, or after planting but before the crop emerges from the soil. If applied postemergence to the crop and/or at layby (the last time machinery can enter the field, as is the case with cotton), crop height restrictions must appear on the labels.

Cyanazine may be formulated for use with fertilizers and/or other herbicides such as atrazine, butylate, alachlor, EPTC, metolachlor or dicamba for use on corn; with norflurazon or MSMA on cotton; with propachlor or propazine on grain sorghum; and with atrazine, paraquat, or 2,4-D on wheat fallow cropland.

Table I-1 shows pesticide products containing cyanazine.

TABLE I-1

PESTICIDE PRODUCTS CONTAINING CYANAZINE

This table includes the following: EPA Registration Number, company name, company address, percentage of cyanazine as an active and type of formulation, such as Granular Product (G), Technical Product (Tech), Wettable Powder (WP), Flowable Concentrate (FlC), Formulation Intermediate (FI), Emulsifiable Concentrate (EmC), and Soluble Concentrate (SoC).

Product Name	% Cyanazine Active	Type Formulation	Reg. No.
Shell BLADEX 80 Wettable Powder Herbicide	80	WP	000201-00279
Shell BLADEX 10-G Granular Herbicide	10	G	000201-00280
Shell BLADEX 4 Water Dispersible Suspension Herbicide	43	FlC	000201-00281
Technical BLADEX Herbicide	94	Tech	000201-00298
BLADEX 15-G Granules Herbicide	15	G	000201-00332
BLADEX 80 Wettable Powder Herbicide for Sorghum	80	WP	000201-00374
BLADEX 80 WP Herbicide for Use on Fallow Cropland	80	WP	000201-00379
BLADEX Herbicide Aqueous Slurry	28.2	FI	000201-00380
BLADEX 80W Herbicide for Cotton	80	WP	000201-00382
BLADEX 4L-W Herbicide	43	FlC	000201-00404
BLADEX 90 DF Herbicide	90	FlC	000201-00414
BLADEX/ATRAZINE (2:1) 80W	53	WP	000201-00403
BLADEX/ATRAZINE 4L	28	EmC	000201-00408
EXTRAZINE 90 DF HERBICIDE	67	G	000201-00420
EXTRAZINE 110DF HERBICIDE	45	SoC	000201-00425

Product Name	% Cyanazine Active	Type Formulation	Reg. No.
EXTRAZINE 110L HERBICIDE	21.5	SoC	000201-00426
EXTRAZINE 310L HERBICIDE	32	SoC	000201-00427
EXTRAZINE 210DF HERBICIDE	60	SoC	000201-00428
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Cropland	80	WP	000201-05696
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Crop Land	80	WP	000201-05697
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Crop Land	80	WP	000201-05698
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Crop Land	80	WP	000201-05699
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Crop Land	80	WP	000201-05700
BLADEX 80 Wettable Powder Herbicide - for Use on Fallow Crop Land	80	WP	000201-05701
BLADEX(R) 4 Water Dispersible Suspension Herbicide	43	FIC	000201-05702
BLADEX 80 Wettable Powder Herbicide for Use on Fallow Crop Land	80	WP	000201-05703
BLADEX 80 Wettable Powder Herbicide for Use on Fallow Crop Land	80	WP	000201-05704
BLADEX 80 Wettable Powder Herbicide for Use on Fallow Crop Land	80	WP	000201-05907
BLADEX 80 Wettable Powder Herbicide	80	WP	000201-05908

Product Name	% Cyanazine Active	Type Formulation	Reg. No.
BLADEX 80 Wettable Powder Herbicide for Sorghum	80	WP	000201-10187
BLADEX 80 Wettable Powder Herbicide for Sorghum	80	WP	000201-10188
BLADEX 80 Wettable Powder Herbicide for Sorghum	80	WP	000201-10248
BLADEX-MSMA Postemergent Herbicide*	17.18	EmC	38167-2
Setre Cyanazine 4L Herbicide*	43	SoC	38167-5
Bladex 80 Wettable Powder* Herbicide	80	WP	38749-10312

Registrants: Shell Chemical Company (Registrant No. 000201)
Agricultural Division
1025 Connecticut Avenue NW., Suite 200
Washington, DC 20036

Setre Chemical Company (Registrant No. 38167)
5100 Poplar, Suite 3200
Memphis, TN 38137

R. F. Lindsey and Sons (Registrant No. 38749)
Route 2
Centre, AL 35960

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* This registration is being cancelled voluntarily.

2. Tolerances

Tolerances ranging from 0.05 to 0.10 ppm have been established for the residues of cyanazine in or on certain raw agricultural food commodities such as corn, cottonseed oil, sorghum, and wheat (see 40 CFR 180.307). Prior to issuance of the cyanazine Registration Standard, an acceptable daily intake (ADI) of 0.006 mg/kg/day had been established for cyanazine, based on a NOEL of 12 ppm (0.6 mg/kg/day) and a toxic endpoint of significant reduction in body weight gain noted in a chronic feeding study in the rat. The customary safety factor of one-hundred-fold was used in setting this ADI, and the maximum permissible intake (MPI) for a 60 kg person was calculated to be 0.360 mg/day (EPA 1984).

The theoretical maximum residue contribution (TMRC) to the human diet as a result of the tolerances given above was expressed in the cyanazine Registration Standard as 0.0175 mg/day/1.5 kg of the diet, or 4.88 percent of the MPI. No tolerances were established for residues of cyanazine in meat, milk, eggs, or poultry because at the time these tolerances were first considered, the parent compound was thought to be the only residue of concern, and it was not present at detectable levels in feed (EPA 1984).

Reevaluation of the chronic feeding study mentioned above revealed major deficiencies that prevent the continued use of this study as a basis for the ADI. Because no other acceptable chronic feeding study was available, the above mentioned ADI could not be recalculated and was considered invalid. Under circumstances such as these, where the ADI cannot be calculated, a provisional acceptable daily intake (PADI) is calculated. The PADI was presented in the cyanazine Registration Standard and is based on a NOEL generated from a subchronic feeding study and a two-thousand-fold margin of safety. A subchronic 13-week feeding study in the rat was used to calculate this PADI. In this study, a NOEL of 25 ppm (1.25 mg/kg) was observed, with a toxic endpoint of organ to bodyweight changes. The PADI was calculated as 0.000625 mg/kg/day and the MPI was calculated to be 0.0375 mg/day for a 60 kg person, based on 1.5 kg diet per day. In this case, although the TMRC would not be changed, the portion of the MPI utilized would be increased from 4.88 percent under the old ADI to 46.66 percent under the PADI.

Since the Registration Standard was issued, Agency policy regarding safety factors has been revised so that the safety factor which should be used in this instance is 1000, instead of 2000. On this basis, the PADI was recalculated to be 0.00125 mg/kg/day and the maximum permissible intake for a 60 kg person would be 0.075 mg/day. On this basis, the existing tolerances would occupy 23.33% of the ADI. (See Chapter II. Section F.1. in this Technical Support Document.)

Because the Agency believes that some of the metabolites of cyanazine may contribute to the overall toxicity levels observed, existing crop tolerances for cyanazine will be recalculated. The new tolerances will be based on the combined residue of the parent cyanazine compound and all metabolites that contain the triazine moiety. Tolerances for meat, milk, eggs, and poultry will be established, if residues of cyanazine and/or its metabolites which contain the triazine moiety are found in animal feed. The Agency has required data sufficient to allow these recalculations, and new tolerances will not be granted until the data are reviewed.

It may be necessary to amend the TMRC, if the contribution to dietary intake is found to be increased by the inclusion of the triazine metabolites. If the combined residue of the parent cyanazine compound and all metabolites that contain the triazine moiety is greater than the residue for cyanazine, alone, the margins of safety for the teratogenic, maternal, and fetotoxic effects, with respect to dietary intake, will be reduced. If the margins-of-safety are unacceptably low, further regulatory action may be found to be necessary.

3. Interim Risk Reduction Measures

Under the registration standard, EPA concluded that cyanazine products should be classified for restricted use. Additionally, the Agency announced that cyanazine labels must include language warning against applying cyanazine where the water table (ground water) is close to the surface and where the soils are very permeable; also, labels were required to state "[t]his product may be hazardous to your health. This product has been determined to cause birth defects in laboratory animals."

II. ASSESSMENT OF RISKS AND ANALYSIS OF PUBLIC COMMENTS

This portion of the Technical Support Document is divided into seven sections. The first section cites the basis for the initiation of the Special Review. The next sections present the developmental toxicity (teratogenic/fetotoxic) risk assessments: section two is hazard identification; section three is dose-response assessment; section four is exposure analysis; and section five is risk characterization. The sixth and seventh sections discuss rebuttal comments concerning teratogenicity and exposure received in response to the Notice of Special Review on cyanazine.

A. Basis of Presumption

The studies summarized in the cyanazine PD 1 and the Registration Standard reported that cyanazine is teratogenic and fetotoxic in laboratory animals. These studies, as well as studies submitted since the issuance of the cyanazine PD 1, are discussed in detail in this Chapter.

B. Hazard Identification

1. Physical - Chemical Properties and Exposure Pathways

Cyanazine* [2-(4-chloro-6-ethylamino-s-triazine 2-ylamino)-2-methylpropionitrile] is a member of a group of herbicides known as s-Triazines. The molecular formula is $C_9H_{13}ClN_6$. The shelf life of formulated cyanazine is greater than two years.

Cyanazine is readily absorbed by roots or foliage, and can be translocated from the roots to the leaves. Its mode of action is through the inhibition of photosynthesis. The use patterns and the environmental behavior of cyanazine suggest that the principal pathways of human exposure are by direct contact during application and ingestion of foodstuffs which contain cyanazine residues; also, cyanazine has been found in ground water and surface water.

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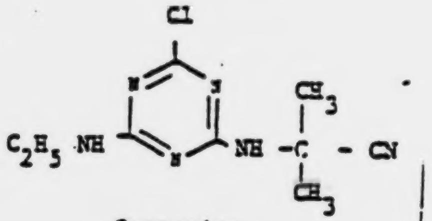
*Has also been known as Bladex, SD 15418, WL 19805, Payze, and Fortrol, and 2-chloro-4-(1-cyano-1-methylethylamino)-6-ethyl-amino-s-triazine.

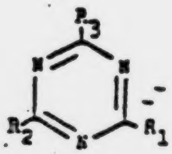
2. Structure - Activity Relationships

The following is the chemical structure of cyanazine:



Cyanazine

The general molecular structure of the s-Triazine herbicide group, of which cyanazine is one, is as follows:



s-triazine

Although other triazine herbicides are not the subject of this Technical Support Document, their structural association with cyanazine deserves attention because cyanazine and the other triazine herbicides have common or similar metabolites which may contribute, individually or collectively, to the teratogenic potential of cyanazine. All triazine herbicides share the same basic structure, that is, they all are trisubstituted s-triazine, and in almost all cases, two of the three substituted groups (R_1&R_2) are alkylamines. The third group (R_3), in most cases, is either chlorine or a thiomethyl group, and in only one case a methoxy group. However, although the third groups (R_3) may seem structurally different, all are similar in size and electronegativity, and ultimately convert biologically to hydroxy groups. In addition to being structurally similar, triazine herbicides undergo similar metabolic pathways (i.e. N-dealkylation, S-dealkylation, O-dealkylation) in addition to reaction with glutathion. These common metabolic pathways result in common or closely similar metabolites. Furthermore, almost all triazines herbicides produce primary amino triazine at one stage or another during the biotransformation process in animals, plants, and soil microflora (EPA, 1984).

Currently there are neither adequate data available to assess the toxicological significance of the metabolic products of cyanazine nor data to dismiss the likelihood of their contribution to the overall toxicity of cyanazine, especially with respect to the teratogenic potential. These data were requested through the Registration Standard issued in December of 1984.

3. Teratogenicity

Agency guidelines specify that teratology testing should be performed in at least two mammalian species, preferably in rats and rabbits (section 83.3 of the subdivision F Guidelines). Shell has submitted teratology studies in both species. Evaluations of these studies are as follows:

a. New Zealand Rabbits

i. Oral Administration

Technical Bladex® (98%) was given to pregnant New Zealand rabbits at 0, 1.0, 2.0, and 4.0 mg/kg/day from days 6-18 of gestation (Shell, 1982). Anorexia, weight loss, death, and abortion were the main maternal effects noted at the 2 and 4 mg/kg dosage levels. Alterations in skeletal ossification sites, decreased litter size, and increases in post-implantation loss were other effects associated with these two dose levels. Malformations were noted at 4 mg/kg and included domed cranium, dilated brain ventricles, anophthalmia, microphthalmia, and thoracoschisis. These anomalies occurred at dosage levels which produced maternal toxicity. The maternal and developmental toxicity NOELs in New Zealand rabbits were established at 1 mg/kg/day.

ii. Dermal Administration

A dermal developmental toxicity study was conducted with the Bladex 4L formulation in pregnant rabbits (Shell^a, 1986). All animals were exposed to 100, 300, 600, or 1000 mg/kg during days 6-18 of gestation. Each day, neck collars were affixed for 6 hours during the exposure period. Significant decreases in maternal weights and food consumption associated with increased incidents of deaths and abortions were noted in all treated groups. Due to a high incidence of maternal loss, the number of litters available for examination was substantially reduced and both the maternal and developmental toxicity NOELs could not be ascertained with confidence.

In a repeat study (Shell^b, 1986) dosage levels of 96, 283, 573, and 955 mg/kg were applied dermally to pregnant rabbits during the period of major organogenesis (days 6-18 of gestation). All animals were restrained in stocks during the daily exposure period (6 hours) and wore a neck collar for the rest of the day. Dermal irritation was noted in all treated animals but significant body weight depressions and food reductions were found only in dams exposed to 283, 573, or 955 mg/kg/day. Evidence of a frank teratogenic effect was not observed in the treated groups; however, the developmental toxic effect of increased incidents of skeletal variations were found at the 955 mg/kg dosage level. Under the conditions of this study, the maternal NOEL was established at < 96 mg/kg (lowest dose tested). A developmental toxicity NOEL was demonstrated at 573 mg/kg.

b. Sprague Dawley Rats

Dose levels of 0, 1, 3, or 30 mg/kg/day were fed to Sprague Dawley rats. Maternal body weight reductions and increased incidents of piloerection were found at the 30 mg/kg dosage level. No developmental toxicity including teratogenicity was demonstrated at any of the dosage levels tested. Based upon these findings, the maternal NOEL was determined to be 3 mg/kg/day with the developmental toxicity NOEL established at >30 mg/kg/day (Shell, 1983).

c. Fischer-334 Rats

The teratogenic potential of technical Bladex® in the Fischer-344 rat was investigated in two feeding studies submitted by the registrant. In the first study (Shell, 1981), dose levels of 0, 1, 2.5, 10, and 25 mg/kg/day were used and maternal body weight reductions during the dosing period were noted at the two highest dosage levels. Diaphragmatic hernia was noted at all dosage levels tested and anophthalmia/micropthalmia was found at the 25 mg/kg dose level. In the absence of acceptable historical control data, the biological significance of these findings could not ~~be~~ ascertained, at that time. To fully evaluate the nature of these findings as well as the survivability of the affected fetuses, a teratology study with a post-natal phase was requested by the Agency.

In the second study (Shell, 1985), dose levels of 0, 5, 25, and 75 mg/kg/day were tested. Dose-related decreases in maternal body weight gains and food consumption as well as increases in clinical manifestations were noted at all dose levels tested. Alterations in skeletal ossification sites were also found at all dose levels used.

Based upon these findings, it was concluded that both a maternal and developmental toxicity NOEL could not be established; therefore, both the maternal and developmental toxicity NOEL were < 5 mg/kg/day (the lowest dose tested). Teratogenic effects were demonstrated at the 75 mg/kg dose level as evidenced by the presence of anophthalmia/microphthalmia, dilated brain ventricles, and cleft palate in the fetuses and abnormalities of the diaphragm in pups sacrificed at weaning.

The diaphragm-related abnormalities were also significantly increased at the 25 mg/kg dose level.

4. Weight-of-the-Evidence

Administration of Bladex by the oral route results in frank teratogenic effects in both rabbits and rats. Anophthalmia and/or microphthalmia was observed in the rabbit at 4 mg/kg (Shell, 1982) and in the Fischer 344 rat at 1 mg/kg (Shell, 1979) and 75 mg/kg (Shell, 1985). Anophthalmia/microphthalmia is thus confirmed in two species by three studies at maternally toxic levels. Dilated brain ventricles were noted in the rabbit at 4 mg/kg (Shell, 1979) and in the Fischer-344 rat at 75 mg/kg (Shell, 1985). Diaphragm related abnormalities were found only in the Fischer 344 rat. In the first study (Shell, 1979), diaphragmatic hernia was found at all dose levels (lowest dose tested = 1 mg/kg). The incidence of diaphragmatic hernia was dose-related except at the lowest dosage level (1 mg/kg) which possibly was increased erroneously by technical errors. In the second study with post-natal investigation (Shell, 1985), "diaphragm central tendon incomplete fusion with raised area of the liver" was increased significantly at the 25 and 75 mg/kg pups sacrificed at weaning. These data, collectively, indicate that abnormalities of the eyes, brain ventricles, and diaphragm may be related to oral administration of Bladex.

The dermal route of exposure does not lead to frank teratogenic effects in rabbits; however, a developmental toxic effect was evidenced by an increase in the incidence of delayed skeletal ossifications was seen in rabbits at 955 mg/kg, the highest dose tested (Shell^b, 1986). The reduced effects seen via the dermal route are probably related to low dermal absorption; only 2% of the applied dose of Bladex was absorbed in a dermal absorption study in rats (Shell^c, 1986).

C. Dose-Response Assessment

As per the Agency's "Guideline for the Health Assessment of Suspect Developmental Toxicants" and the Office of Pesticide Programs' "Standard Evaluation Procedure for Teratology", a no-observed-effect-level (NOEL) from an oral developmental toxicity study should be used to assess the developmental potential hazard of dietary exposures, and when available, a dermal NOEL from a dermal developmental toxicity study should be used for workers-loaders-applicators when their exposures are primarily dermal, as is the case with cyanazine.

With respect to developmental toxicity, the New Zealand rabbit apparently is the most sensitive species. The developmental toxicity NOEL for oral administration was established at 1 mg/kg/day (Shell, 1982) and the developmental toxicity NOEL for dermal administration was determined to be 573 mg/kg/day (Shell^b, 1986). These two NOELs are used to determine the margins-of-safety of cyanazine for dietary and non-dietary exposure, respectively. (See sections F.1.b. and E.1. in this Chapter.)

D. Exposure Assessment - Non-dietary Exposure to Cyanazine

The Agency has evaluated various exposure studies to estimate mixer/loader and applicator exposure to cyanazine, including a study submitted by a cyanazine registrant, Shell Chemical Co. Cyanazine is formulated as a liquid, wettable powder, and a dry flowable granular. The liquid formulation accounts for 75% of cyanazine products (Shell, 1985).

Agency usage information on cyanazine indicates that 95% of cyanazine is used on corn compared to 3% on cotton, 1% on sorghum and <1% on wheat fallow. Ground boom application accounts for the vast majority of applications. Aerial application is less than 1% and center pivot irrigation is minimal.

Because cyanazine is a suspect human teratogen, exposures are expressed on a daily basis. The Agency assumes that the average individual at potential risk is a 60 kg woman. Exposure values are not adjusted for the dermal absorption of cyanazine through the skin.

1. Ground Boom Application To Field Crops

Agency usage information indicates that the recommended broadcast rates to corn range from 1.25 to 4.75 lbs a.i./acre. Recommended rates on cotton range from 0.5 to 1.3 lbs a.i./acre for preemergence and 0.6 to 1.6 lbs a.i./acre for post emergence use. On wheat fallow the recommended rates range from 2.4 to 3.2 lbs a.i./acre and on milo from 0.8 to 1.6 lbs a.i./acre.

Assuming that an individual will work 10 hours during the day of application, a total of 140 acres can be treated daily. Based on this acreage and the previously described application rates, the total pounds of active ingredient handled per day are as follows:

a. Corn - 175 to 665 lbs a.i./day

b. Cotton - 70 to 224 lbs a.i./day

c. Wheat Fallow - 366 to 448 lbs a.i./day

d. Milo - 112 to 224 lbs a.i./day

Two exposure studies were evaluated by EPA. The Shell study measured the exposure to three individuals mixing, loading, and applying Baldex 4L to corn (Shell, 1985). All individuals wore protective gloves during mixing/loading functions. Mixing and loading was done by pouring Bladex 4L® from the container into the spray tank (i.e. the open pour method). Two individuals applied cyanazine with closed cab tractors and the third individual used an open cab tractor. EPA estimates that the dermal exposure to individuals mixing, loading, and applying cyanazine with a closed tractor cab was 0.20 ug/kg/lb a.i. and that respiratory exposure was 0.3 ug/kg/lb a.i. The estimated exposure when the open cab tractor was used was 1.3 ug/kg/lb a.i. via the dermal route and 5.0 ug/kg/lb a.i. via the respiratory route. The estimates for the closed tractor cab were based on eight replicates and the estimates for the open tractor cab were based on four replicates. Therefore, this study, which was submitted by Shell, was used for the Agency's exposure estimates when protective gloves, only, are used and when both protective gloves and a closed tractor cab are used.

The second study entitled "Spray Operator Safety Study" was conducted by the British Agrochemicals Association Limited (BAAL, 1983). The herbicide 2,4-D was applied to grassland using an enclosed tractor with open windows with mounted hydraulic or controlled droplet boom sprayers. A total of six replicates for each of three individuals was studied. Protective gloves were not worn and all dermal exposure measurements were exterior to the clothing. Table II-1 presents the dermal exposure estimates. The dermal exposure estimates to the arms, torso, and legs have been reduced by 50% to estimate the effect of long sleeve shirts and long legged pants on dermal exposure. Potential inhalation exposure could not be estimated because most samples were below the 15 ug/filter level of detection. The dermal exposure for combined mixing/loading and application for the three individuals averaged 83, 150 and 120 ug/kg/lb a.i. The average for the 18 replicates was 120 ug/kg/lb a.i. The hands accounted for the majority of the total exposure. Therefore, this surrogate* study was used for the Agency's exposure estimates when no protective gloves are used.

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*Surrogate data is an acceptable method of estimating exposure. Numerous exposure studies over the last 3 decades have demonstrated that exposure is not chemical specific. It is dependent on formulation type, method of application, and application rate. In the presence of data on the specific chemical, the Agency will consider all available data, including surrogate data, to reach an appropriate regulatory position.

Daily dermal exposure estimates are presented in Table II-2. The use of protective gloves during mixing/loading reduces the daily exposure. Respiratory exposure is approximately three orders of magnitude less than the dermal exposure and is, therefore, considered relatively insignificant.

TABLE II-1

BAAL STUDY DERMAL EXPOSURE ESTIMATES

DERMAL EXPOSURE (MG/OPERATION)

	WORKER #1		WORKER #2		WORKER #3	
Body Area	M/L[a]	Application	M/L	Application	M/L	Application
Chest	0.84	0.57	4.0	0.61	0.21	0.58
Back	0.13	0.34	0.24	0.28	0.07	0.25
Arms	3.0	0.81	6.3	2.5	2.1	2.1
Hands	92	20	190	26	114	78
Thighs	0.80	0.78	5.2	1.0	0.49	1.8
Shins	0.24	2.5	13	1.7	0.82	0.77
Combined[b] Total (mg)	122		251		201	
lbs a.i. handled	24.64		28.49		28.16	
Exposure (mg/lb a.i)	4.95		8.81		7.14	
Exposure (mg/kg/lb a.i.)	0.0825		0.147		0.119	

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[a] M/L = mixing/loading

[b] Combine = M/L + Application

TABLE II-2

CYANAZINE EXPOSURE DURING GROUND BOOM USES

exposure per lb. a.i.[a] for stated condition x lbs. handled in the[b] stated operation = exposure

a. CORN

i. Protective Gloves During Mixing/Loading and Enclosed Tractor Cab

Low Application Rate = 35 ug/kg/day

High Application Rate = 135 ug/kg/day

ii. Protective Gloves During Mixing/Loading and Open Tractor Cab

Low Application Rate = 230 ug/kg/day

High Application Rate = 860 ug/kg/day

iii. No Protective Equipment and Open Tractor Cabs

Low Application Rate = 21,000 ug/kg/day

High Application Rate =80,000 ug/kg/day

b. COTTON

i. Protective Gloves During Mixing/Loading and Enclosed Tractor Cab

Low Application Rate =14 ug/kg/day

High Application Rate =45 ug/kg/day

[a] See page II-7

[b] See page II-7

(TABLE II-2 continued)

ii. Protective Gloves During Mixing/Loading and Open Tractor Cab

Low Application Rate =91 ug/kg/day

High Application Rate =290 ug/kg/day

iii. No Protective Equipment and Open Tractor Cabs

Low Application Rate =8,400 ug/kg/day

High Application Rate =27,000 ug/kg/day

c. Wheat Fallow

i. Protective Gloves During Mixing/Loading and Enclosed Tractor Cab

Low Application Rate = 67 ug/kg/day

High Application Rate = 90 ug/kg/day

ii. Protective Gloves During Mixing/Loading and Open Tractor Cab

Low Application Rate = 440 ug/kg/day

High Application Rate = 580 ug/kg/day

iii. No Protective Equipment and Open Tractor Cabs

Low Application Rate = 40,000 ug/kg/day

High Application Rate = 54,000 ug/kg/day

(TABLE II-2 continued)

d. Milo

i. Protective Gloves During Mixing/Loading and Enclosed Tractor Cab

Low Application Rate = 22 ug/kg/day

High Application Rate = 45 ug/kg/day

ii. Protective Gloves During Mixing/Loading and Open Tractor Cab

Low Application Rate = 150 ug/kg/day

High Application Rate = 290 ug/kg/day

iii. No Protective Equipment and Open Tractor Cabs

Low Application Rate = 13,000 ug/kg/day

High Application Rate = 27,000 ug/kg/day

2. Aerial Application To Crops

Agency usage information indicates that aerial application of cyanazine to corn is relatively uncommon. Furthermore, although cyanazine is registered for aerial application to cotton, grain sorghum, and wheat fallow, there is no usage information available which shows that cyanazine is being applied aerially to these crops. If cyanazine is applied aerially, the Agency assumes that the acreage covered daily will range from 250 to 600 acres with 400 acres likely. The actual spray time required will range from 2.5 to 4.5 hours/day with 3.0 hours likely.

The Agency has evaluated three surrogate exposure studies (Lavy, et al., 1982; Peoples, et al., 1979; Dubelman et al., 1982) in which dermal exposure to mixer/loaders wearing gloves and using closed loading systems was evaluated. Based on 20 replicates from the three studies, the dermal exposure is estimated to be 0.38 ug/kg/lb a.i. The Agency does not have sufficient data to estimate exposure to mixer/loaders using a closed system without protective gloves or using the dry flowable. In addition, based on data in the Lavy (1982) and BAAL studies, the dermal exposure to mixers/loaders wearing gloves and doing open pour loading is 16 ug/kg/lb a.i. Furthermore, the BAAL, Lavy, and Dubelman, studies were evaluated to estimate dermal exposure to mixer/loaders using open pour loading without protective gloves. Based on 25 replicates in these three studies, the dermal exposure was estimated to be 75 ug/kg/lb a.i. during open pour without gloves.

A total of 29 replicates from six studies were evaluated by the Agency to estimate dermal exposures to pilots. The mean dermal exposure to pilots from the six studies was as follows:

Lavy (1982)	5.3 ug/kg/hr
Lavy (1980)	6.8 ug/kg/hr
Maddy (1981)	0.5 ug/kg/hr
Peoples (1979)	16 ug/kg/hr
Mumma (1985)	17 ug/kg/hr
Atallah (1982)	6.3 ug/kg/hr

The exposure estimates presented above were adjusted to an application rate of 1.0 lb a.i./acre. The weighted average for dermal exposure to pilots is 11 ug/kg/hr.

Cyanazine exposure during aerial application is given in Table II-3.

TABLE II-3

a. Grain Sorghum

i. Mixer/Loader Exposure Using No Protection for Aerial Application to Grain Sorghum

Low Usage: 0.80 lbs a.i./acre x 250 acres/day = 200 lbs a.i./day; 200 lbs a.i./day x 75 ug/kg/lb a.i. = 15 mg/kg/day

Likely Usage: 1.5 lbs a.i./acre x 400 acres/day = 600 lbs a.i./day; 600 lbs a.i./day x 75 ug/kg/lb a.i. = 45 mg/kg/day

High Usage: 3.2 lbs a.i./acre x 600 acres/day = 1920 lbs a.i./day; 1920 lbs a.i./day x 75 ug/kg/lb a.i. = 140 mg/kg/day

ii. Mixer/Loader Exposure Using Protective Gloves for Aerial Application to Grain Sorghum

Low Usage: 0.80 lbs a.i./acre x 250 acres/day = 200 lbs a.i./day; 200 lbs a.i./day x 16 ug/kg/lb a.i. = 3.2 mg/kg/day

Likely Usage: 1.5 lbs a.i./acre x 400 acres/day = 600 lbs a.i./day; 600 lbs a.i./day x 16 ug/kg/lb a.i. = 9.6 mg/kg/day

High Usage: 3.2 lbs a.i./acre x 600 acres/day = 1920 lbs a.i./day; 1920 lbs a.i./day x 16 ug/kg/lb a.i. = 31 mg/kg/day

iii. Mixer/Loader Exposure Using a Closed System and Protective Gloves for Aerial Application to Grain Sorghum

Low Usage: 0.80 lbs a.i./acre x 250 acres/day = 200 lbs a.i./day; 200 lbs a.i./day x 0.38 ug/kg/lb a.i. = 76 ug/kg/day

Likely Usage: 1.5 lbs a.i./acre x 400 acres/day = 600 lbs a.i./day; 600 lbs a.i./day x 0.38 ug/kg/lb a.i. = 230 ug/kg/day

High Usage: 3.2 lbs a.i./acre x 600 acres/day = 1920 lbs a.i./day; 1920 lbs a.i./day x 0.38 ug/kg/lb a.i. = 730 ug/kg/day

(TABLE II-3 continued)

b. Corn

i. Mixer/Loader Exposure Using No Protection Preemergent Aerial Application to Corn

Low Usage: 0.62 lbs a.i./acre x 250 acres/day = 155 lbs a.i./day; 155 lbs a.i./day x 75 ug/kg/lb a.i. = 11.6 mg/kg/day

Likely Usage: 2.5 lbs a.i./acre x 400 acres/day = 1000 lbs a.i./day; 1000 lbs a.i./day x 75 ug/kg/lb a.i. = 75 mg/kg/day

High Usage: 6.0 lbs a.i./acre x 600 acres/day = 3600 lbs a.i./day; 3600 lbs a.i./day x 75 ug/kg/lb a.i. = 270 mg/kg/day

ii. Mixer/Loader Exposure Using Protective Gloves Preemergent Aerial Application to Corn

Low Usage: 0.62 lbs a.i./acre x 250 acres/day = 155 lbs a.i./day; 155 lbs a.i./day x 16 ug/kg/lb a.i. = 2.5 mg/kg/day

Likely Usage: 2.5 lbs a.i./acre x 400 acres/day = 1000 lbs a.i./day; 1000 lbs a.i./day x 16 ug/kg/lb a.i. = 16 mg/kg/day

High Usage: 6.0 lbs a.i./acre x 600 acres/day = 3600 lbs a.i./day; 3600 lbs a.i./day x 16 ug/kg/lb a.i. = 58 mg/kg/day

iii. Mixer/Loader Exposure Using a Closed System and Gloves for Preemergent Aerial Application to Corn

Low Usage: 0.62 lbs a.i./acre x 250 acres/day = 155 lbs a.i./day; 155 lbs a.i./day x 0.38 ug/kg/lb a.i. = 59 ug/kg/day

Likely Usage: 2.5 lbs a.i./acre x 400 acres/day = 1000 lbs a.i./day; 1000 lbs a.i./day x 0.38 ug/kg/lb a.i. = 380 ug/kg/day

High Usage: 6.0 lbs a.i./acre x 600 acres/day = 3600 lbs a.i./day; 3600 lbs a.i./day x 0.38 ug/kg/lb a.i. = 1370 ug/kg/day

(TABLE II-3 continued)

iv. Mixer/Loader Exposure Using a Closed System and Gloves for Postemergent Aerial Application to Corn

Low Usage: 1.2 lbs a.i./acre x 250 acres/day = 300 lbs a.i. day; 300 lbs a.i./day x 0.38 ug/kg/lb a.i. = 114 ug/kg/day

Likely Usage: 2.0 lbs a.i./acre x 400 acres/day = 800 lbs a.i./day; 800 lbs a.i./day x 0.38 ug/kg/lb a.i. = 300 ug/kg/day

High Usage: 3.12 lbs a.i./day x 600 acres/day = 1873 lbs a.i./day; 1872 lbs a.i./day x 0.38 ug/kg/lb a.i. = 710 ug/kg/day

c. Wheat Fallow

i. Mixer/Loader Exposure Using No Protection for Aerial Application to Wheat Fallow

Low Usage: 1.6 lbs a.i./acre x 250 acres/day = 400 lbs a.i./day; 400 a.i./day x 75 ug/kg/lb a.i. = 30 mg/kg/day

Likely Usage: 2.8 lbs a.i./acre x 400 acres/day = 1120 lbs a.i~~./day;~~ 1120 lbs a.i./day x 75 ug/kg/lb a.i. = 84 mg/kg/day

High Usage: 4.0 lbs a.i./acre x 600 acres/day = 2400 lbs a.i./day; 2400 lbs a.i./day x 75 ug/kg/lb a.i. = 180 mg/kg/day

ii. Mixer/Loader Exposure Using Protective Gloves for Aerial Application to Wheat Fallow

Low Usage: 1.6 lbs a.e./acre x 250 acres/day = 400 lbs a.e./day; 400 a.i./day x 16 ug/kg/lb a.i. = 6.4 mg/kg/day

Likely Usage: 2.8 lbs a.i./acre x 400 acres/day = 1120 lbs a.i./day; 1120 lbs a.i./day x 16 ug/kg/lb a.i. = 18 mg/kg/day

High Usage: 4.0 lbs a.i./acre x 600 acres/day = 2400 lbs a.i./day; 2400 lbs a.i./day x 16 ug/kg/lb a.i. = 38 mg/kg/day

(TABLE II-3 continued)

iii. Mixer/Loader Exposure Using a Closed System and Gloves for Aerial Application to Wheat Fallow

Low Usage: 1.6 lbs a.i./acre x 250 acres/day = 400 lbs a.i./day; 400 a.i./day x 0.38 ug/kg/lb a.i. = 150 ug/kg/day

Likely Usage: 2.8 lbs a.i./acre x 400 acres/day = 1120 lbs a.i./day; 1120 lbs a.i./day x 0.38 ug/kg/lb a.i. = 430 ug/kg/day

High Usage: 4.0 lbs a.i./acre x 600 acres/day = 2400 lbs a.i./day; 2400 lbs a.i./day x 0.38 ug/kg/lb a.i. = 910 ug/kg/day

d. Pilot Exposure During Application to Grain Sorghum

Low Usage: 11 ug/kg/hr x 0.80 x 2.5 hrs/day = 22 ug/kg/day

Likely Usage: 11 ug/kg/hr x 1.5 x 3.0 hrs/day = 50 ug/kg/day

High Usage: 11 ug/kg/hr ~~x 3.2~~ x 4.5 hrs/day = 160 ug/kg/day

e. Pilot Exposure During Preemergent Application to Corn

Low Usage: 11 ug/kg/hr x 0.62 x 2.5 hrs/day = 17 ug/kg/day

Likely Usage: 11 ug/kg/hr x 2.5 x 3.0 hrs/day = 83 ug/kg/day

High Usage: 11 ug/kg/hr x 6.0 x 4.5 hrs/day = 300 ug/kg/day

f. Pilot Exposure During Postemergent Application to Corn

Low Usage: 11 ug/kg/hr x 1.2 x 2.5 hrs/day = 33 ug/kg/day

Likely Usage: 11 ug/kg/hr x 2.0 x 3.0 hrs/day = 66 ug/kg/day

High Usage: 11 ug/kg/hr x 3.12 x 4.5 hrs/day = 150 ug/kg/day

g. Pilot Exposure During Application to Wheat Fallow

Low Usage: 11 ug/kg/hr x 1.6 x 2.5 hrs/day = 44 ug/kg/day

Likely Usage: 11 ug/kg/hr x 2.8 x 3.0 hrs/day = 92 ug/kg/day

High Usage: 11 ug/kg/hr x 4.0 x 4.5 hrs/day = 200 ug/kg/day

3. Chemigation

Agency usage information indicates that chemigation to corn accounts for less than 1% of cyanazine application to corn. Corn is the only crop for which chemigation is listed on the label as an application method. Cyanazine would most likely be pumped from a bulk tank or 55 gallon drum into a nurse tank. A mixer/loader may also empty 50 lb bags of the dry flowable formulation into a nurse tank. Open pour from 5 gallon containers is less likely because it would take too much time if containers were used that held only 5 gallons. The use of chemigation with cyanazine appears to be extremely limited,and reliable data describing the common practices for mixing and loading cyanazine for chemigation do not exist. For risk assessment purposes, the Agency assumed that the boom length on the irrigation pipe averages 1,320 feet and treats 126 acres. The application rate averages 3.0 lbs a.i./acre but ranges from 1.2 to 4.8 lbs a.i./acre. The total pounds a.i. used to treat the 126 acres averages 378 pounds and ranges from 158 to 604 lbs a.i.

As discussed under aerial application, the Agency used three surrogate studies in which dermal exposure to mixers/loaders, while wearing gloves and using closed loading systems, was evaluated (Lavy, et al., 1982; Peoples, et al., 1979; Dubelman, et al., 1982). As given for aerial application, the dermal exposure is estimated to be 0.38 ug/kg/lb a.i., based on 20 replicates from these three studies. (Sufficient data are not available to estimate exposure ~~to~~ mixers/loaders who use closed systems but no protective gloves or use the dry flowable.)

Also, as in the Agency's exposure assessment for aerial application, three surrogate exposure studies were evaluated to determine dermal exposure to mixer/loaders not wearing gloves and using open pour loading (Lavy, et al., 1982; Dubelman, et al., 1982; BAAL, 1983). Based on the data in these three studies, the dermal exposure to mixer/loaders not wearing gloves and using open pour loading is 75 ug/kg/lb a.i. In addition, based on data in the Lavy-82 and BAAL studies, the dermal exposure to mixer/loaders wearing gloves and open pour loading is 16 ug/kg/lb a.i.

Table II-4 presents the estimated dermal exposure for mixer/loaders with chemigation. Chemigation does not require the use of an applicator.

Table II-4

CYANAZINE EXPOSURE DURING CHEMIGATION

a. Open Pour/No Gloves

LOW: 158 lbs a.i./day x 75 ug/kg/lb a.i. = 12000 ug/kg/day

MEAN: 378 lbs a.i./day x 75 ug/kg/lb a.i. = 28000 ug/kg/day

HIGH: 604 lbs a.i./day x 75 ug/kg/lb a.i. = 45000 ug/kg/day

b. Open Pour/Gloves

LOW: 158 lbs a.i./day x 16 ug/kg/lb a.i. = 2,500 ug/kg/day

MEAN: 378 lbs a.i./day x 16 ug/kg/lb a.i. = 6,000 ug/kg/day

HIGH: 604 lbs a.i./day x 16 ug/kg/lb a.i. = 9,700 ug/kg/day

c. Closed System/Gloves

LOW: 158 lbs a.i./day x 0.38 ug/kg/lb a.i. = 60 ug/kg/day

MEAN: 378 lbs a.i./day x 0.38 ug/kg/lb a.i. = 140 ug/kg/day

HIGH: 604 lbs a.i./day x 0.38 ug/kg/lb a.i. = 230 ug/kg/day

E. Risk Characterization - Non-dietary Risks

Risks presented by teratogenic chemicals, such as cyanazine, are expressed in terms of "margins-of-safety" (MOS). The margin of safety is defined as the ratio of the "no-observed-effect-level" (NOEL) to exposure. The risk posed by a teratogen is considered to be "one hit"; that is, being exposed once to a teratogen may result in teratogenic effects. Generally, the Agency becomes concerned when the margin-of-safety for a particular use is below 100. Margins-of-safety greater than 100 provide reasonable assurance that persons are unlikely to be at risk, taking into consideration the uncertainty resulting from extrapolation of animal data to humans, and the variations in sensitivity among humans.

The following formula was used to calculate the margins-of-safety for non-dietary exposure to cyanazine:

$$\text{Margin-of-Safety} = \frac{\text{Dermal Developmental Toxicity NOEL(1)}}{\text{Exposure level (2)}}$$

(1) 573 mg/kg/day (Shell^b, 1986)
(2) See Tables II-2-3, and -4 in this Chapter

Developmental toxicity risk assessments for ground boom application, aerial application, and chemigation are presented in Table II-5.

TABLE II-5

a. Ground Boom Application

	Margins of Safety	
	Low Rate Applicator Exposure	High Rate Applicator Exposure
i. CORN		
No protective equipment, open tractor cab	27	7
Protective gloves, open tractor cab	2490	670
Protective gloves, enclosed tractor	16370	4240
ii. COTTON		
No protective equipment, open tractor cab	68	21
Protective gloves, open tractor cab	6300	1980
Protective gloves, enclosed tractor	40930	12730

(TABLE II-5 continued)

iii. WHEAT FALLOW		
No protective equipment, open tractor cab	14	11
Protective gloves, open tractor cab	1300	990
Protective gloves, enclosed tractor	8550	6370
iv. MILO		
No protective equipment, open tractor cab	44	21
Protective gloves, open tractor cab	3820	1980
Protective gloves, enclosed tractor	26050	12730

b. Aerial Uses	Low Rate Applicator Exposure	High Rate Applicator Exposure
Applicator (Pilot)		
i. Grain Sorghum:	—	320
ii. Corn:	—	170
iii. Wheat Fallow:	—	250
Mixer/Loader		
i. Grain Sorghum:		
Without protective gloves	25	5
With protective gloves	115	24
With protective gloves/closed system	4780	1000
ii. Corn		
Without protective gloves	48	2
With protective gloves	230	11
With protective gloves/closed system	9710	440
iii. Wheat Fallow		
Without protective gloves	15	2
With protective gloves	71	12
With protective gloves/closed system	3015	520
c. Chemigation		
i. Open Pour - No protective gloves	48	13
ii. Open Pour - Protective gloves	230	59
iii. Protective gloves - Closed system	9550	2490

Protective gloves significantly reduce total dermal exposure and the accompanying risk because the hands receive the largest percentage of the dermal exposure. Franklin, C. (Occupational Exposure to Pesticides and Its Role in Risk Assessment Procedures Used in Canada, Dermal Exposure Related to Pesticide Use, 1985 American Chemical Society, Symposium Series #273, pg. 429-444) reviewed a variety of exposure studies and determined that hand exposure accounted for 52 to 99% of the total dermal exposure during mixing/loading. A closed loading system is a mechanical method of transfering the concentrated pesticide from the container to the mix tank. By eliminating exposure due to splashing of the concentrate onto the mixer/loader and reducing other means of contact with the concentrate, the closed system greatly reduces mixer/loader exposure and, thus, risk.

F. Other Possible Exposure Concerns

1. Dietary

a. Exposure

Dietary exposure to cyanazine and its metabolites may occur through ingestion of cyanazine-treated crops. Tolerances for cyanazine are published under CFR 180.307 and are established for residues of cyanazine in or on the following raw agricultural commodities:

Commodities	Tolerances (ppm)
Corn, all types	0.05 ppm
Cotton seed	0.05 ppm
Sorghum	0.05 ppm
Wheat	0.10 ppm

However, these tolerances are established and expressed in terms of residues of the parent compound (cyanazine), only; none of the metabolites are included. The Agency believes that residues of the metabolites of cyanazine containing the triazine moiety (e.g., chloro- and hydroxytriazine metabolites) are of concern and must be included in crop tolerances. (See Chapter I.C.2. and section II.B.2. in this Chapter.)

The major plant metabolites of cyanazine have been identified, and their distribution in various plants was determined. Most of these metabolites are present in treated plants at levels higher than cyanazine itself (EPA, 1984). Residues of the parent compound were found to constitute less than 2% of the total residue, and at harvest the residues of cyanazine in corn did not exceed 3.3 to 10.5% of the total residue based on the type of soil (EPA, 1984).

Cyanazine metabolites triazine moiety were not included in the current cyanazine tolerance expression. The Agency is currently reassessing cyanazine tolerances, and revised tolerances for cyanazine will be based on the combined residue of the intact triazine herbicide and its metabolites containing the triazine moiety. Also, because cyanazine residues of the parent compound only constituted a negligible portion of the dietary burden of cattle, no tolerances were required for animal products; see 40 CFR 180.6(a)(b). The reassessment of cyanazine tolerances to include residues of the metabolites containing the triazine moiety might therefore require that tolerances for meat, milk, poultry, and eggs be established. Additional animal metabolism data are needed, as well.

b. Risks

The developmental toxicity risk assessment for cyanazine dietary exposures is calculated using the following equations:

$$\text{Exposure} = \frac{\text{Maximal Serving size}^{a} \text{ x Tolerance}}{\text{Average weight of females of child bearing age}^{b}}$$

(a) Maximal serving size from the Food Buying Guide, USDA, 8/77

(b) 54.8 kg used by the Tolerance Assessment System, USEPA.

$$\text{Margin of Safety} = \frac{\text{Developmental Toxicity NOEL}^{c}}{\text{Exposure}}$$

(c) Oral NOEL = 1 mg/kg/day

CORN:

Maximal serving size/day = 65 grams
Tolerance = 0.05 ppm
Exposure = 0.00006 mg/kg/day
Margin of safety = 16,666

WHEAT:

Maximal serving size/day = 114 grams
Tolerance = 0.1 ppm
Exposure = 0.00021 mg/kg/day
Margin of safety = 4760

SORGHUM: (syrup)

Maximal serving size/day = 0.45 grams
Tolerance = 0.05 ppm
Exposure = .0004 ug/kg/day
Margin of safety = greater than 100,000

39

COTTON SEED: (oil)
Maximal serving size/day = 2.25 grams
Tolerance = 0.05 ppm
Exposure = .002 ug/kg/day
Margin of safety = greater than 100,000

These margins of safety are calculated on the basis of cyanazine residues only. At harvest, residues of cyanazine constitute a very small portion of the total toxic residue. As previously discussed above, the cyanazine metabolites containing the triazine moiety will be included in the revised tolerance expression. Therefore, the margins-of-safety for dietary exposure will be recalculated based on the combined residues of cyanazine and its metabolites containing the triazine moiety; combined residues may increase the dietary exposure estimate, resulting in developmental toxicity margins-of-safety which will be lower than those given above.

2. Ground water and Surface Water

Cyanazine has been found in ground water and surface water. Currently, the major registrant for cyanazine, Shell Chemical Company, is conducting monitoring studies; all such data are required to be submitted to the Agency by January 1987.

When applied to soils, cyanazine is degraded by either soil microflora or other environmental factors to other forms of triazine degradates and metabolites which are similar to those metabolites found in plants [EPA (Toxicology Chapter), 1984]. Although cyanazine dissipates fairly rapidly in soils (EPA, 1984), the triazine moiety-containing metabolites might persist in soils for relatively long periods of time. Soil metabolites of cyanazine are very likely to be more polar than cyanazine, itself, and thus, more water soluble. Some of the cyanazine metabolites were detected in the runoff water at levels similar to or greater than the parent compound [EPA (Toxicology Chapter), 1984] suggesting a greater mobility of these metabolites in soil. Therefore, leaching is also likely to occur, resulting in contamination of ground water. With the growing toxicological concern for triazine metabolites, the potential for leaching of cyanazine and its metabolites will be further examined to confirm or alleviate this concern as ground water which is contaminated with cyanazine and its metabolites may be used as drinking water.

3. Spray Drift

The Agency has reviewed surrogate exposure studies in which flagger exposure was determined. The Lavy, Maddy, Peoples, and Atallah studies measured dermal exposure to 24 flagger replicates. Flaggers are in the field during application and would receive the greatest exposure from the spray drift. The overall mean dermal exposure from the flagger studies indicated an average exposure of 3.8 mg/hr at an application rate of 1.0 lb a.i./acre.

Under the highest use scenario, cyanazine is applied at 5.6 lbs. a.i./acre for 4.5 hours. This would yield an exposure of 1.6 mg/kg/day with a margin-of-safety (MOS) of 360. This use pattern is unlikely. The Drug Enforcement Agency investigated spray drift from the application by aircraft of the herbicide glyphosate (Final Environmental Impact Statement - Cannabis Eradication on Non-Federal and Indian Lands in the Contiguous United States and Hawaii, May 1986, U.S. Department of Justice, Drug Enforcement Agency, pp. D-4 to D-6). The spray drift deposited 82 feet from the line of flight was 0.98% of the application rate. During a High Drift scenario the deposition of spray 164 feet from the line of flight was 3.0% of the application rate. The 0.98% deposition occurs at wind speeds of 9 mph with D6 nozzles oriented back with the airstream. The 3.0% deposition occurs at wind speeds of 7 mph with D4 nozzles pointed down.

Assuming that the 3.0% deposition occurs at 164 feet, an individual would receive a dermal exposure of 1.6 mg/kg/day x 0.03 = 0.048 mg/kg/day which yields a MOS of over 1000. Based on this worst case scenario spray drift exposure does not appear to be a concern. However, if different application practices were followed, exposure could be much higher.

4. Secondary Exposure

The possibility of secondary exposure exists from the handling of clothing worn during cyanazine use or from the cross-contamination of household laundry when previously uncontaminated household laundry is washed with contaminated work clothing. Data do show that cross-contamination does occur when contaminated clothing are washed with household clothing during common laundering; however, EPA does not have data to quantify the dose of cyanazine which would be received by a launderer or a person using items washed with cyanazine contaminated items.

G. Analysis of Rebuttal Comment Concerning Teratogenic Effects

1. Rebuttal Comment 1:

First, a cyanazine registrant, Shell Oil Company, stated that the only exposure to cyanazine of concern is the dermal exposure during mixing, loading, and applying the test material. The registrant recognized the potential developmental toxicity of cyanazine and agreed that, at that time, the rabbit NOEL of 1 mg/kg should be used in the risk estimates. Second, the registrant provided examples of their calculated margins-of-safety for workers with and without protective clothing and indicated that wearing of protective clothing is unwarranted.

Agency Response:

First, additional data have been submitted by Shell since the receipt of Shell's responses to the cyanazine Notice of Special Review. Two dermal developmental toxicity studies in rabbits were submitted (Shell[a], 1986; Shell[b], 1986) and reviewed by the Agency. From these studies, a dermal developmental toxicity NOEL was established at 573 mg/kg and this NOEL was used in the risk estimates for workers-loaders-applicators who are primarily exposed to cyanazine by the dermal route of exposure. The rabbit oral NOEL of 1 mg/kg, referred to by Shell in the above rebuttal comment, was used by the Agency to calculate the risk associated with dietary exposures (Shell 1982). Second, the margins-of-safety for workersloaders-applicators were calculated by the Agency using exposure data provided partially by Shell. Agency calculations show that adequate margins of safety are obtained when protective gloves are worn during mixing and/or loading for ground boom use and when both protective gloves and closed loading systems are used during mixing and/or loading for aerial application and chemigation. (Shell's margins-of-safety were based on Shell's, combining exposure from open and enclosed tractor cabs, and the Agency separated these scenarios in its calculations.)

H. Analyses of Rebuttal Comments Concerning Exposure

1. Rebuttal Comment 1:

The major registrant, Shell, did not believe that surrogate exposure data should be used.

Agency Response:

Shell stated concern over the use of the BAAL study with 2,4-D as a surrogate for cyanazine exposure. The BAAL study demonstrates exposure when using no protective clothing or protective gloves and using an open tractor cab. This is a worst-case exposure. In conducting the exposure assessment for this Technical Support Document, the Agency used the Shell exposure study to estimate exposure under two scenarios: 1) use of protective gloves during mixing/ loading and use of an enclosed tractor cab and 2) use of protective gloves during mixing/loading and use of an open tractor cab.

Numerous exposure studies over the last 3 decades have demonstrated that exposure is not chemical specific. It is dependent on formulation type, method of application, and application rate. Therefore, the use of surrogate data is an acceptable method of estimating exposure (Field Worker Exposure: The Usefulness of Estimates Based on Generic Data, Honeycutt, R.C., Dermal Exposure Related to Pesticide Use, American Society of Chemistry Symposium Series 273, 1985, pg. 369-375). This is especially true where no data exist on the particular chemical being examined. In the presence of data on the specific chemical, the Agency will consider all available data, including surrogate data, to reach an appropriate regulatory position.

2. Rebuttal Comment 2:

Mr. John Datt, Executive Director of the American Farm Bureau Federation, submitted a letter dated 28 May 1985 stating the Federation's concern with the Special Review of cyanazine. Mr. Datt urged a prompt and expeditious review of cyanazine.

Agency Response:

The Agency appreciates the concern for a prompt and expeditious review. A thorough evaluation of mixer/loader and applicator exposure to cyanazine has been conducted as part of the Special Review.

3. Rebuttal Comment 3:

Mr. Ellery Knake, Chairman of the Pesticide Impact Assessment Committee, University of Illinois and Weed Science Society of America Representative to the Council for Agricultural Science and Technology, submitted comments concerning the use of cyanazine in Illinois. Mr. Knake provided usage information concerning cyanazine and stated that the number of women handling cyanazine is small. Mr. Knake recommended a label warning on cyanazine products stating that women should not be exposed to the product during pregnancy. He also recommended that improvement in training programs for applicators be emphasized.

Agency Response:

Mr. Knake's comments and information are appreciated. The usage information was considered along with other sources of usage information in conducting the exposure analysis.

The Agency is aware of the need to improve applicator training. Currently, EPA is working with State regulatory officials and the USDA Cooperative Extension Service to improve federally-mandated training programs.

III. BENEFITS SUMMARY

A. Introduction

The Agency has conducted an analysis of the benefits of cyanazine which is summarized in this section. The analysis indicates those benefits which would be lost to the users, and any other affected groups, should cyanazine uses be limited or totally cancelled. Information used in the analysis was derived from several sources, including scientific literature, the cyanazine Registration Standard, published state recommendations, company submitted data, various USDA reports, and telephone conversations with various university cropping experts throughout the country.

B. Ground Boom Application

1. Corn

The largest use of cyanazine is on corn, accounting for about 95 percent of its total annual usage. Approximately 4.6 million acres of corn (14 to 16% of the total U.S. corn acreage) were treated in 1982 with cyanazine as the sole active ingredient. Cyanazine is used on corn at a rate of 1.25 to 4.75 lbs a.i. per acre, depending on soil type and organic content. (Cyanazine is registered for use on corn for postemergence grass control at 6 lbs a.i. per acre; however, in actual practice, rates above 2.5 lbs a.i. per acre are rarely used due to possible phytotoxicity. Also, such postemergence grass control is less than 5% of cyanazine usage on corn.) It is estimated that about 20-35 percent of the total cyanazine applications to corn are made at rates in excess of 2.5 lbs a.i. per acre. When cyanazine is tank mixed with other herbicides, the cyanazine use rate drops, and cyanazine usage at less than 2.5 lbs a.i. per acre (80-65 percent) is primarily tank mixed with atrazine and/or the grass herbicides, alachlor, metolachlor, pendimethalin, EPTC, or butylate.

Cyanazine is applied to corn as a preemergence or postemergence broadcast application by ground equipment in the spring. Growers selected cyanazine over other currently available corn herbicides for: (1) its wide broadleaf and annual grassy weed control spectrum; (2) the wide number of herbicides it can be tank mixed with to further increase its weed control spectrum; (3) its ability to reduce the carry-over effect of other triazine herbicides on subsequent crops and (4) its lack of crop rotational restrictions.

A limited number of corn herbicides are registered which control as wide a spectrum of weeds as cyanazine. Atrazine is the major alternative to cyanazine for pre- or postemergent control. Also, atrazine is the most widely used herbicide on corn; however, residues may carry over in the soil to the next crop and limit the growers' options for rotational crops. Because of its short residual life, cyanazine has no crop rotational restrictions and is often tank mixed with atrazine so that the amount of atrazine used will be reduced and thus, the carry-over effects will be reduced. The ratio of cyanazine:atrazine varies from 3:1 where more grass control and less triazine carry-over is desired, to 1:1 where broadleaf control is more important and carry-over is less of a concern. The use of this tank mix has been gaining in popularity among growers because of the broad spectrum of weed control obtained relative to the cost of the application. This tank mix combination is used at cyanazine rates both above and below the 2.5 lb a.i./acre rate.

Cyanazine is reported to be better than alachlor for the control of grasses and is often recommended when grassy weeds are a concern. Atrazine does not adequately control foxtail and other annual grasses (e.g. crabgrass, fall panicum) at lower rates or under low rainfall conditions as well as does cyanazine. Other herbicides which compete with cyanazine are simazine, a tank mix of butylate and atrazine, and package mixes of metolachlor and atrazine and atrazine and propachlor. These alternatives have a smaller weed control spectrum, and those mixed with atrazine still produce a carryover effect. Simazine is less flexible in its application timing than cyanazine as are tank mixes of butylate and atrazine and a package mix of atrazine and propachlor. The butylate and atrazine mixture has regional restrictions which cyanazine does not. The package mix of metolachlor and atrazine also provides less control of certain broadleaf weeds than does cyanazine.

The use of cyanazine at rates in excess of 2.5 lb a.i./acre is generally on high organic matter soils (over 3%) and on soils with a pH greater than 7.0. These soil characteristics, particularly if associated with calcareous (limestone) deposits, preclude the use of atrazine.

The following geographic areas have been identified where cyanazine is the only available preemergence control for the grass/broadleaf weed complex.

1. North Central Iowa - 3.8 million acres of corn/soybeans on the Clarion-Nicollet-Webster soil association. Of this association, approximately 1 million acres are highly calcareous (limestone deposits) on which atrazine cannot be used.

2. S.E. Minnesota - 2.14 million acres of corn/soybeans on the Clarion-Nicollet-Webster soil association. Of these soils, approximately 0.25 million acres are highly calcareous on which atrazine cannot be used.

3. Parts of WI, MI, NY, PA - 500,000 acres in WI and 15,000 acres in PA. Treatment acres were not available for MI or NY. Cool/wet soils and calcareous soils preclude the use of atrazine, thus creating a reliance on cyanazine at high rates.

4. Blackland Soils in TX - 80,000 acres on which atrazine cannot be used. Without cyanazine growers would experience up to 10 percent yield losses due to uncontrolled cocklebur, sunflower, and morningglory. State laws do not allow the use of 2,4-D and dicamba at this time of the year due to the close proximity of cotton.

The Agency assumes that the overall impacts from cancellation of cyanazine use on corn would be low due to the availability of the registered alternatives: atrazine; alachlor; simazine; and package mixes of metolachlor and atrazine, and atrazine and propachlor. There could be significant impacts to individual users in areas where the soil has a pH of 7 or more.

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligible. The proposed label modifications are not expected to pose hardships.

2. Wheat Fallow

There is relatively little usage of cyanazine to control weeds in wheat fallow. Only 10 percent of the country's 20 to 25 million acres of wheat fallow is chemically treated for weed control. Of this 10 percent, about 150,000 to 200,000 acres receive cyanazine applications. Therefore, cyanazine applications treat only 1 percent of the U.S. total wheat fallow acreage.

The intent of using crop rotations which include a fallow period is to build up a reserve of soil moisture and nutrients for the succeeding crop, which would result in an increased yield. Controlling weeds during the fallow period is critical in order to keep the moisture in the soil. The use of herbicides for this weed control is increasing because it helps to minimize the number of tillage operations that would otherwise be needed. This not only helps to conserve soil moisture and nutrients, but but also reduces soil loss from wind and water erosion. Fuel consumption, equipment wear, and labor are also minimized.

Mechanical tillage is still the most common form of weed control used in a fallow cropping rotation, ranging from 50-90 percent of the total fallow acres in various states. Although it is not highly recommended by the weed control experts, the growers are hesitant to change practices with depressed wheat prices supplying only marginal profits.

Reasons for moving away from mechanically tilled fallow involve direct and indirect costs, and can be readily outlined. The costs associated with additional passes across the field (4-8 possible) include those for fuel, equipment wear, labor, and soil loss from wind or water erosion. When combined with data indicating potential soil moisture savings with chemical fallow (between 0.5-2.0 inches) and yield increases of 4-7 bushels/acre for each additional inch of soil moisture, there is a potential benefit of a 2-14 bushel/acre yield increase through the use of chemical fallow.

Cyanazine is valuable in most wheat fallow programs involving chemical use because of its broad spectrum weed control and short term soil residual activity. Since typical conditions in fallow regions often include low rainfall, high soil pH, short growing season, and highly variable soil conditions across fields, the short soil residual of cyanazine becomes critical in minimizing phytotoxicity to the following wheat crop. The aforementioned climatic and soil conditions all favor herbicide longevity in the soil and promote crop phytotoxicity from highly persistent chemicals such as atrazine.

Atrazine is a soil active herbicide that, unlike cyanazine, is highly persistent. Under those conditions that favor herbicide persistence, it is often still available in the soil at the fall planting of the wheat, resulting in crop phytotoxicity. It can sometimes be applied at reduced rates to minimize the carry-over problem, but weed control consequently becomes less reliable.

Growers currently using cyanazine in wheat fallow, typically apply it as a tank mix with atrazine. This combination offers the grower a number of benefits including (1) broadening the weed control spectrum over that of either chemical applied alone, (2) minimizing atrazine carry-over and resultant crop phytotoxicity without sacrificing weed control, and (3) reducing the cost of cyanazine applied alone through its direct replacement with a small amount of the less expensive atrazine. A likely dosage would include 1.5-2.0 lb ai/acre of cyanazine in combination with 0.5 lb ai/acre of atrazine.

The weed control spectra of cyanazine and atrazine are generally considered to be similar. Cyanazine does not provide good control of pigweed but generally provides better control of grasses, especially fall panicum and crabgrasses.

The long term losses from soil erosion are not readily quantified, but are important to the continued productivity of the land. These soil losses can also be minimized with the use of chemical fallow.

The cost of a typical tank mix application of cyanazine plus atrazine ranges from $10.75 to $12.95 per acre. The chemical alternatives alone and in various combinations range in cost from $5.20 to $23.67 per acre. The mixture of cyanazine and atrazine provides a broad spectrum of weed control relative to the cost. In order to obtain a similar spectrum of control, current cyanazine users would most likely use another combination of the alternatives which at maximum, would cost roughly $12 more per acre. Mechanical tillage costs an estimated $4.00 per pass per acre, and 4 to 6 passes ($16-$24) are generally required to maintain weed control. If with an application of cyanazine plus atrazine a farmer can reduce the number of mechanical tillage operations by three, he would recover the cost of the chemical application. In addition, by reducing tillage, the retention of soil moisture and nutrients would increase, resulting in increased yields of 2-14 bushels per acre, and increased gross revenues of $5.00 to $35.00 per acre.

As indicated earlier, there is relatively little usage of cyanazine to control weeds in wheat fallow. Only 10 percent of the total estimated U.S. wheat fallow is chemically treated for weed control, with only about 10 percent of the total chemically treated fallow land treated with cyanazine. If cyanazine was cancelled for use on wheat fallow, some impact on current individual users might result; however, the overall impact would be insignificant.

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligible. The proposed label modifications are not expected to pose hardships.

3. Cotton

In cotton, cyanazine may be applied preemergent, directed early postemergent or as a layby (late) postemergent directed treatment. It can be tank mixed with norflurazon as a preemergent treatment or with MSMA as a postemergence directed spray. Both cyanazine and the tank mix with norflurazon are recommended as the best treatment for spotted spurge control. Possible alternatives to cyanazine use in cotton would be prometryn, fluometuron, and diuron; however, cyanazine is registered for control of more weeds than any of the other three herbicides.

Diuron has more rotational crop restrictions than does cyanazine. Approximately 84 percent of the cyanazine used on cotton is reported to be applied as a directed postemergence treatment. The remaining 16 percent is applied as preemergent treatments.

Overall impacts from cancellation of cyanazine use on cotton would be insignificant due to the very low usage on cotton (3% or less) and availability of the registered alternatives; prometryn, fluometuron and diuron.

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligible. The proposed label modifications are not expected to pose hardships.

4. Grain Sorghum

Cyanazine may be applied to grain sorghum as a preemergent application but only when tank mixed with propachlor or with propazine. These tank mixes cannot be used on sand, sandy loam, loamy sand, and peat or muck soils. Also, these tank mixes have several geographical restrictions because of possible crop injury under stress conditions. Potential alternatives to cyanazine include propachlor and atrazine as a tank or package mix, and the package mix of metolachlor and atrazine. These alternatives except for propachlor also carry crop rotational or regional restrictions. The cyanazine tank mixes appear to control more broadleaf weeds than the alternatives. Generally, the tank mix of cyanazine and propazine is believed to give better control of broadleaf weeds than the cyanazine and propachlor tank mix. However, cyanazine tank mixes are generally less effective on cocklebur and morningglory.

Overall impacts from cancellation of cyanazine use on grain sorghum would be insignificant due to the very low usage on this crop (less than 1%) and availability of the registered alternatives; atrazine and propachlor.

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligible. The proposed label modifications are not expected to pose hardships.

C. Cyanazine Application Via Chemigation

Extensive contacts with state and industry sources indicated no significant amount of cyanazine application via chemigation. Therefore, there would be little or no impact from cancellation of this use.

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligiable. The proposed label modifications are not expected to pose hardships.

D. Cyanazine Application Via Aerial Equipment

Very little aerial application of cyanazine occurs; it is relatively easy for a grower to apply preemergent herbicides during other cultural operations, and cyanazine is most frequently applied to all sites as a preemergent control. The major registrant, Shell, estimates that a total of 70,000 acres of corn are treated aerially with cyanazine. (There are no data showing that cyanazine is being applied aerially to cotton, wheat fallow, or sorghum.)

If modifications to the label were made, to comply with the Agency's proposed regulatory action (see Chapter IV), the impact on benefits would be negligible. The proposed label modifications are not expected to pose hardships.

E. Analysis of Rebuttal Comments Concerning Benefits

Rebuttal comment #1: Importance in California corn and cotton production.

Harold A'ford, the regional coordinator for the University of California's Cooperative Extension Service, cites the usage of cyanazine in CA corn and cotton production. He outlines the major alternatives for these uses and their respective weaknesses.

Agency response: EPA agrees with those benefits cited.

Rebuttal comment #2: Importance in Georgia corn and cotton production and in South Carolina corn production.

James F. Miller, the Head of the Extension Agronomy Department at the University of Georgia College of Agriculture, cites the usage of cyanazine in corn silage short-term rotation by dairymen because of its short soil residual. Usage in cotton and reduced tillage corn was also mentioned as having importance.

Joe Zublena, Corn Extension Agronomist for Clemson University, cites the value of cyanazine's short soil residual in crop rotations to sensitive crops like vegetables and tobacco. He also refers to cyanazine's postemergent burn-down activity as being beneficial under certain management conditions. A regional assessment for corn and soybeans in the southeastern states was included for Agency use.

Agency response: EPA agrees with those benefits cited, and refers repeatedly to the value of cyanazine's short soil residual to rotated crops in its benefits analysis.

Rebuttal comments #3-42: Importance in the following productions: corn; grain sorghum; wheat fallow; cotton; irrigated field corn; sweet corn; rotational crop; silage corn; and no-till corn, and the importance to Kansas conservation tillage and chemical fallow systems.

Clyde C. Dowler, Research Agronomist at the USDA Coastal Plain Experiment Station, cites the value of cyanazine's short soil residual to multiple crop rotations after a corn crop. He also cites cyanazine's broad spectrum of weed control and the cost advantages that are associated with not having to use a combination of other chemicals to achieve the same level of control.

Erick B. Nilson, Herbicide Extension Specialist at Kansas State University, cites that cyanazine's major uses in KS are in corn, grain sorghum, and in reduced tillage programs. It is most important because of its short soil residual. No other short residual herbicide exists for corn and grain sorghum weed control.

Everett Leach, the Director of Agronomy Tech/Sales Administration for Land O'Lakes, Inc., cites that cyanazine is an economical way to control grasses and weeds in corn. Its short residual is valuable in minimizing atrazine carryover when applied in tank mix with the more residual atrazine.

Arnold P. Appleby, Professor of Crop Science at Oregon State University, cites the value of cyanazine's short soil residual to both wheat fallow and corn. The light soils and low rainfall in eastern OR make atrazine use too dangerous to the succeeding crop.

Richard Behrens, Professor of Weed Science at the University of Minnesota, cites the importance of cyanazine usage on over 1 million acres of corn in MN. This is mainly used in southwestern and western MN where the use of atrazine is limited because of soil residual carry-over problems. Cyanazine is also widely used throughout the state in tank mixes with grass herbicides to control certain atrazine-tolerant, troublesome grasses; treatments without cyanazine do not provide adequate control of these grasses. For those acres which require an early post-emergent, follow-up treatment, cyanazine is the only alternative in western MN because of the atrazine residue problem.

W.M. Lewis, a Crop Science Extension Specialist at North Carolina State University, cites the importance of cyanazine's short soil residual to rotational crops like fall-planted small grains or alfalfa, and spring-planted peanuts, soybeans, and tobacco. Dairy farmers use cyanazine in corn silage to allow double cropping in the fall with small grains for a second silage crop, or to alfalfa. In no-till corn, cyanazine supplies both burn-down activity on existing vegetation, and residual weed control.

Bill B. Fischer, Farm Advisor for Fresno County, CA, cites the value of cyanazine in CA cotton and corn production. Cyanazine is applied early preplant (prior to preirrigation) instead of paraquat and glyphosate to eliminate the risk from the drift of these chemicals. Cyanazine controls certain weeds in cotton that are not controlled by the commonly used dinitroaniline class of herbicides. Cyanazine is important in corn rotations because of the long soil residual of the other triazine herbicides. Restrictions on the use of phenoxy herbicides between March 15 and October 15 due to the proximity of susceptible crops, eliminates the use of 2,4-D in CA corn.

Stephen D. Miller, Associate Professor of Weed Science at the University of Wyoming, cites cyanazine's relatively broad spectrum of weed control and short soil residual as being important to WY corn rotations and wheat fallow. The high soil pH (7.2 to 8.5), limited rainfall, and limited growing season due to the high elevation, are all factors which favor triazine herbicide persistence in the soil.

Jim Nelson, Extension Weed Specialist at Montana State University, cites that a loss of cyanazine would impact the farmer through higher product costs, increased production costs, limited crop rotations from persistent soil residues, decreased yields due to crop phytotoxicity or reduced weed control, and through limited cropping practices.

Harold M. Kempen, Farm Advisor for Kern County, CA, cites cyanazine's broad spectrum of weed control and short soil residual as being critical to rotating from cotton to other crops. It controls nightshade and annual morning glory, which are missed by the existing residual herbicides in the dinitroaniline class.

David Van Der Puy, Extension Weed Specialist for North Dakota State University, cites cyanazine's broad spectrum of weed control and its short soil residual as being important to crop rotations. He also cites the alternative herbicides in corn and their weaknesses.

Robert Parker, Extension Weed Scientist at Washington State University, cites that cyanazine's broad spectrum of weed control and short soil residual are important to their irrigated corn production. Their coarse, low organic soils can provide conditions for atrazine residues to the potatoes that usually follow in rotation. The postemergent broadleaf herbicides, 2,4-D and dicamba require a separate spray application, and require precise timing to obtain control; spray drift is always a concern. The amount of corn injury is unacceptable to some growers from 2,4-D if conditions are favorable for crop injury and the time of application. 2,4-D's lack of soil residual does not control weeds which germinate after treatment. Cultivation can only be used for weed control for a short period after crop emergence, is expensive in time and equipment, has to be repeated, and can damage the corn's root system.

Robert G. Wilson, Weed Specialist at the University of Nebraska, cites cyanazine's short soil residual and relatively broad spectrum of weed control as being important to western NE corn rotations to triazine sensitive crops. The generally high pH soils in that part of the state enhance atrazine carry-over, and rates of 1 lb/A or more will injure sensitive rotational crops. Without cyanazine, growers would have to rely on postemergence broadleaf herbicides which would generally not be as effective, and would cause greater potential for corn injury.

Arthur H. Lange, Extension Weed Scientist at the University of California, cites the short soil residual of cyanazine as being important to CA sweet corn rotational crops. The lighter soils in the area allow for too much atrazine carry-over and resultant crop injury to rotated crops.

Russell S. Moomaw, Extension Crops & Weeds Specialist at the University of Nebraska, cites cyanazine's short soil residual as being important to corn crop rotations in northeast NE's diversified crop and livestock producing area. Atrazine is effective, but has crop rotation limitations which are a serious concern in their area. 2,4-D and dicamba are only considered to be supplements rather than replacements for herbicides like cyanazine. Loss of cyanazine would bring about the use of more mechanical tillage operations which would be a serious reversal in efforts to preserve their soil resource through reduced or conservation tillage.

Gordon Roskamp, Associate Professor at Western Illinois University, cites cyanazine's importance to both no-till and conventional-till corn. Its most likely alternative, atrazine, is quite persistent in the soil, and will injure soybeans grown in rotation. The rate of atrazine that is needed to give consistent weed control will carry over in the next year's soybean crop, so cyanazine is often recommended to make up the additional triazine herbicide beyond that atrazine level which will not carry over. Cyanazine is the only short residual herbicide that will control giant foxtail, the worst weed in row crops in IL. Giant foxtail has been shown to reduce corn yields between 25 and 100 percent, depending on the severity of the infestation. Cultivation is not an effective alternative for the control of this weed in corn.

Phillip Stahlman, Weed Control Research Scientist at Kansas State University, cites cyanazine's importance to conservation tillage and chemical fallow systems. Its short soil residual allows the farmer the option of planting corn or grain sorghum a few weeks after a cyanazine application, or continuing the fallow period and planting winter wheat in the fall. Most other available herbicides either lack residual properties in the soil or persist too long limiting cropping options.

Stanley Heathman, Extension Weed Specialist at the University of Arizona, cites cyanazine's short soil residual as being important in both corn and cotton production. It also controls Hyssop spurge in cotton which is not well controlled with diuron or prometryn. Hand hoeing would have to be used for this weed if cyanazine were not available.

Scott Hagood, Extension Weed Scientist at Virginia State University, cites cyanazine's short soil residual as being critical to corn rotation to no-till forage legumes and other triazine sensitive crops. Cyanazine also demonstrates good burn-down and residual control in no-till corn production. Potential early preplant use in soybeans to control horseweed has been studied and has shown promising results on a weed that is somewhat tolerant to paraquat.

Harry Agamalian, Farm Advisor for Monterey County, CA cites cyanazine's short soil residual as being important to a grower's ability to rotate to other crops.

Frank Webb, Extension Weed Control Specialist at the University of Delaware, cites cyanazine's use in no-till corn production as being critical to this cropping practice in their state. Its burn-down and soil residual activity are something that no other single chemical offers.

Robert J. Meyer, of Weed Control Management, Inc., cites cyanazine use in cotton as being important for controlling winter weeds in the fallow beds. It produces excellent weed control, is affordable, and does not injure the following crops.

Peter K. Fay, Associate Professor of Agronomy at Montana State University, cites cyanazine's broad spectrum of weed control and short soil residual as being critical to their ability to grow rotational crops after corn. Their colder, longer winters and alkaline soils do not allow for the use of the more residual triazines such as atrazine. A loss of cyanazine would require the use of a number of other chemicals to obtain the same level of control.

Vivan M. Jennings, Associate Director of the Iowa Cooperative Extension Service, cites cyanazine's broad weed control spectrum and short soil residual as being important to corn production in a number of ways. The other readily available triazine, atrazine, is often too persistent, causing severe carry-over problems to succeeding crops. This is particularly true when soil pH levels are high and soil moisture levels are low, resulting in incomplete breakdown. Cyanazine's short residual also makes replanting of crops in the current year a possibility. The use of IPM is increasing, and practices such as scouting are not possible without chemicals like cyanazine that can be used successfully after the scouting operation. Cyanazine is one of the few postemergence herbicides that will control both grasses and broadleaf weeds in emerged corn. Alternatives like 2,4-D and dicamba, although effective on broadleaf weeds, have no activity on grasses. Both of these chemicals may have undesirable vapor drift problems that will damage nearby broadleaf crops.

Fred W. Roeth, Professor of Agronomy (Weed Science) at the University of Nebraska, cites cyanazine's short soil residual as being important to the ability to maintain a corn/soybean rotation. It is usually used to complement atrazine rates, thereby reducing the total atrazine rate without sacrificing weed control. The direct substitution for atrazine on a pound-per-pound basis gives this combination an advantage over other herbicide combinations where different modes of action are involved. It is also valuable in complimenting the thiocarbamate herbicides for shattercane control without the necessity of increasing the thiocarbamate rates. It is the only herbicide that can be used after corn and shattercane emergence to aid in its control. A loss of cyanazine would lead to increased atrazine usage which would reduce crop rotation. Crop rotation has a very favorable effect on weed control, crop culture, and insect control. Continuous corn culture increases shattercane and corn insect and disease problems. They do not want to move back to this practice.

Marshal D. McGlamery, Professor of Weed Science and Extension at the University of Illinois, cites cyanazine's short soil residual as being important to their ability to rotate from corn to soybeans or alfalfa. Its control of giant foxtail, fall panicum, and crabgrass which is better than that of atrazine or simazine is important since giant foxtail is the most prevalent weed in IL corn fields. Cyanazine is primarily tank mixed with the available grass herbicides and/or with atrazine in a 2-way or 3-way combination to reduce the risk of atrazine carry-over. Other broadleaf controls without carry-over risk are 2,4-D, dicamba, and bromoxynil which are all applied postemergence. These require an extra application; 2,4-D and dicamba present problems with drift to nearby susceptible drops; and bromoxynil is a contact herbicide that must be applied earlier and with fairly high water volumes.

Russel R. Hahn, Sr. Extension Associate at Cornell University, cites cyanazine's early postemergence control of emerged annual grasses such as crabgrass and fall panicum, as well as its short soil residual, and its use as a contact herbicide in no-till corn, as all being important to corn production in NY. He estimates that 20-25% of the approximately 1.3 million acres of field corn in NY is treated with cyanazine.

Paul VanDerSchaaf, President of VanDerSchaaf Agricultural Research Inc., cites cyanazine's minimal drift damage potential, short soil residues, and reasonable cost as all being important to midwest field corn production.

George Kapusta, Professor at Southern Illinois University, cites cyanazine's broad spectrum of weed control, short soil residue, reasonable cost, and use early preplant in conservation tillage as all being important to midwestern crop production.

Leo E. Bendixen, Professor at Ohio State University, cites cyanazine's short soil residual and relatively broad spectrum of weed control as being important to Ohio corn production.

David R. Pike, Pesticide Impact Assessment Program Coordinator at the University of Illinois, cites cyanazine's broad spectrum of weed control (especially of fall panicum and emerged foxtails), and its short soil residual allowing for crop rotations as being important to Illinois corn production. Maintaining crop rotations has permitted farmers to reduce or eliminate insecticide use and has allowed farmers to rotate herbicides for more efficient weed control, and reduce the possibility of the development of resistant weed strains.

Gene Arnold, Professor of Plant Science at South Dakota State University, cites cyanazine's usage in SD on approximately 20% of its 2.5 million acres of corn. It is also used somewhat on sorghum and wheat fallow, on around 20,000 acres of each. Cyanazine's short soil residual allows for cropping rotations.

J.B. Weber, Professor of Weed Science at North Carolina State University, cites cyanazine's excellent contact activity as a postemergence herbicide, and annual broadleaf and grass control when applied preemergence in conventionally-tilled crops, its short soil residual, and good weed control in conservation-tillage corn as all being important to their cropping practices.

Michael D.K. Owen, Associate Professor of Extension Weed Science at Iowa State University, estimates that 30-45% of Iowa's 14,000,000 acres of corn are treated with cyanazine. The broad weed control spectrum and short soil residual make its use important to cropping rotations. The Clarion-Nicollette-Webster soil is a major association in IA in which soil pH is above 7.0-7.5. Atrazine carries over in this soil making rotations to soybeans impossible. On other soils in the state, atrazine rates have to be reduced to avoid carry-over; to avoid a resultant lack of efficacy, atrazine is tank mixed with cyanazine to retain a certain triazine level. Cyanazine can be applied either preemergent or postemergent to the crop and weeds. There are other herbicides that can be applied postemergence, but none will control both grasses and broadleaf weeds as does cyanazine. Cyanazine use in reduced tillage and no-till corn is important to the continued progress towards reduced soil erosion, water contamination, etc. Alternative herbicide regimes are likely to be more costly.

Harold D. Coble, Professor of Weed Science at North Carolina State University, cites cyanazine's shorter soil residual as being critical to the NC corn/tobacco rotation which is so prevalent in the state. Its use in no-till corn is also important because of its good burn down and residual control . eliminating the need for multiple herbicide mixtures that would be necessary with the alternatives.

A.D. Cole, Senior Agronomist for CENTROL Cooperative, cites cyanazine's short soil residual as being important to crop rotations. Rotations to alfalfa and grasses also reduce soil losses via good groundcover.

Alan C. York, Crop Science Extension Specialist at North Carolina State University, cites their light soil texture as eliminating preemergence use of cyanazine. It is important as a directed postemergence application, especially for the control of morningglory. It is sometimes tank mixed with MSMA for this use. Its short soil residual is also important in that peanuts often follow cotton in rotation, and can be injured by some of the alternatives.

Ellery L. Knake, Chairman of the Pesticide Impact Assessment Committee at the University of Illinois, and the Weed Science Society of America's Representative to the Council for Agricultural Science and Technology, provided a short history of herbicidal use in corn. Within this, he gave the pros and cons of both atrazine and cyanazine use, and those related to their use together in a tank mix. The benefits associated with cyanazine usage have to do with its short soil residual allowing for the safe rotation between corn and soybeans, the broad weed spectrum (especially when tank mixed with atrazine), the control of particular problem weeds (velvetleaf, fall panicum, bur cucumber, etc.), its postemergence weed control in corn, and its use in conservation tillage programs (burn down plus residual control).

Robert Gordon Harvey, Professor of Weed Science at the University of Wisconsin, cites cyanazine's broad weed control spectrum (especially when tank mixed with atrazine), short soil residual in relation to rotational crops, and ability to control particular problem weeds (sometimes in tank mixes) as being important to corn production in WI. Chemical alternatives were discussed, as was their timing, level of control, potentials for corn phytotoxicity, drift to adjacent sensitive crops, need for additional passes, incorporation, etc.

Agency response: EPA agrees with those benefits cited and refers to those which are applicable in its benefits analysis.

IV. REGULATORY OPTIONS AND RISK/BENEFIT ANALYSIS

A. Introduction

FIFRA requires the Agency to weigh the risks against the benefits for the pesticide uses of concern to determine whether continued registration would cause unreasonable adverse effects on health or the environment. In Chapter II the Agency described the risks posed to applicators, mixers and loaders who are exposed to cyanazine from agricultural use. In Chapter III the Agency identified the major alternative pesticides to the uses of cyanazine and described the benefits from the use of cyanazine.

To determine whether continued registration of cyanazine is appropriate, this Chapter reviews the Agency's conclusions concerning the risks and benefits from cyanazine use. This Chapter also identifies the regulatory options available to the Agency to reduce the risks from cyanazine use. Each option has been evaluated for impact on the risks and benefits of the registered uses of cyanazine, and the most appropriate option has been proposed.

B. Risk Conclusions

Data reviewed by the Agency show that cyanazine produces developmental toxic effects in rabbits and rats. Exposure to applicators, mixers and loaders was identified as the occupational exposure of concern. The degree of risk varies, depending on on the use rate and the number of acres treated (see Chapter II.B, C, and D).

Margins-of-safety from the ground boom use of cyanazine were found to be unacceptable unless protective gloves were used during mixing and loading operations and when adjusting, repairing or cleaning equipment during or following ground boom application (see Chapter II.E). In addition, the use of a chemical resistant apron is proposed to be required during mixing and loading operations. Accidental spills may occur during such operations, and it is common for mixers and loaders to lean against the tanks during mixing and loading operations. Therefore, although the risks which result from dermal exposure when leaning against the tanks or when accidental spills occur cannot be quantified, they may be significant in light of the developmental toxic effects of cyanazine.

Margins-of-safety from chemigation and aerial use of cyanazine were found to be unacceptable unless protective gloves and a closed loading system were used (see Chapter II.E). Product formulations which cannot be used in a closed loading system would have to prohibit aerial use and chemigation. In addition, due to the potential exposure resulting from possible ruptured hoses and other closed system failures or from leaning against mixing tanks, the use of a chemical resistant apron is proposed to be required during mixing and loading operations.

The Agency has found that secondary exposure may also occur when contaminated clothes are brought home. Although data are not available to quantify such exposure, data do show that cross-contamination does occur when contaminated clothes are washed with household laundry; (see Chapter II.F.) Separate laundering would prevent that contamination.

Because hands receive the largest percentage of the dermal exposure during mixing/loading, it is assumed that the protective gloves will be contaminated on the outside with a large percentage of the cyanazine being handled; (see Chapter II.E.) Washing protective gloves with soap and water after use and before being removed from the hands would reduce exposure that might occur when contaminated gloves are handled after use.

C. Benefits Conclusions

There are several registered, alternative pesticides to cyanazine for ground boom use on sorghum, cotton, and wheat fallow, as well as mechanical tillage for weed control in wheat fallow. There are several registered, alternative pesticides for use on corn at the lower use rates (<2.5 lbs a.i. per acre). The Agency assumes that those alternatives could be used with no significant increase in production costs. For rates above 2.5 lbs a.i. per acre, atrazine is the only available alternative for ground boom use on corn to control some weeds, and under certain conditions, atrazine cannot be used. (See Chapter III.B.)

Overall impacts from cancellation of cyanazine for ground boom use on corn, cotton, wheat fallow, and grain sorghum would be low to moderate due to the availability of the registered alternatives. There could be significant impacts to individual users in areas where alternatives cannot be used for various reasons (e.g. soil pH, crop rotational restrictions).

If modifications to the label were made for ground boom use which require: 1) the use of of protective gloves; 2) use of chemical resistant aprons; 3) separate laundering of cyanazine contaminated clothes; and 4) washing of protective gloves, the impact on benefits would be negligible. These protective measures are inexpensive. Therefore, the proposed label modifications are not expected to pose hardships.

Preemergent chemicals are rarely applied aerially because it is relatively easy for a grower to apply these types of herbicides during other agricultural operations. Approximately 70,000 acres of corn are treated aerially. There are no data showing that cyanazine is being applied aerially to cotton, wheat fallow, or sorghum. No significant usage of cyanazine through chemigation has been reported.

Overall impacts from cancellation of cyanazine for aerial use and chemigation would be low. If modifications to the label were made requiring: 1) the use of protective gloves; 2) a closed loading system (and the labels of product formulations which cannot be used in a closed loading system would contain language prohibiting the use of those formulations in aerial application and chemigation); 3) use of chemical resistant aprons; 4) separate laundering of cyanazine contaminated clothes; and 5) washing of protective gloves, the impact on benefits would be negligible. The Agency assumes that all of these protective measures are inexpensive; requiring a closed loading system is expected to have minimal impact. Information from the National Agricultural Aviation Association indicates that most aerial operators currently handle pesticides with some form of mechanical transfer. Therefore, the proposed label modifications are not expected to pose hardships.

D. DEVELOPMENT OF REGULATORY OPTIONS

Three options for regulating cyanazine have been examined. They are:

Option 1 - Continuation of Registration without Changes

Option 2 - Continuation of Registration Provided There are Modifications to the Terms and Conditions of Registration

Option 3 - Cancellation of Registration

The regulatory options specified below are based on the assumption that registered products containing cyanazine are in compliance with Agency regulatory positions announced in the cyanazine Registration Standard.

Adoption of Option 1 is only appropriate when the Agency has concluded that the level of risk is acceptable in light of the benefits and that future risk reduction measures are not necessary to assure that the use of the pesticide meets the statutory standard for continued registration. The Agency has concluded that the risks posed by use of cyanazine, based on the current registrations, outweigh the benefits from its use.

Adoption of Option 3, cancellation, is only appropriate when the Agency has concluded that the risks from a use outweigh the benefits of that use, and that these risks cannot be mitigated to an acceptable level, in light of the benefits, by any other measures short of cancellation. The Agency believes that the risks presented by the use of cyanazine can be mitigated without cancellation by modifiying the terms and conditions of the registration.

Adoption of Option 2 is appropriate when the risks of a pesticide use can be reduced to a level where the benefits of use outweigh the risks. The Agency believes that the risks posed by the use of cyanazine can be lowered to acceptable margins by modifying the terms and conditions of registration as follows:

1. Ground Boom Application

The Agency believes that the risks from ground boom application can be lowered to acceptable margins if protective gloves are worn when mixing or loading cyanazine or when adjusting, repairing, or cleaning equipment, and a chemical resistant apron is worn during mixing and loading operations.

2. Aerial Application and Chemigation

The Agency believes that the risks posed by cyanazine use for both aerial application and chemigation can be lowered to acceptable margins if protective gloves and a chemical resistant apron are worn and a closed loading system is used. Product formulations which cannot be used in a closed loading system would have to prohibit aerial use and chemigation.

3. Secondary Exposure

The Agency believes that secondary exposure may also occur when contaminated clothes are brought home. Although data are not available to quantify such exposure, data do show that cross-contamination does occur when contaminated clothes are washed with household laundry. Therefore, the Agency proposes that a precaution against washing contaminated clothing with other household laundry be added to the label.

4. Washing of Protective Gloves

Because hands receive the largest percentage of the dermal exposure during mixing/loading, it is assumed that the protective gloves will be contaminated on the outside with a large percentage of the cyanazine being handled. Therefore, the Agency is proposing that language be added to all cyanazine labels which states that protective gloves must be washed with soap and water after use and before being removed from the hands.

5. Restricted Use

All cyanazine products have been required to be classified for restricted use. Furthermore, Agency policy states that when a pesticide is classified for restricted use, the reason for that classification must be printed in the "Restricted Use" statement which appears on the label. Therefore, all cyanazine labels would have to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water.

E. SUMMARY OF PROPOSED DECISION

The Agency is proposing that cyanazine registrations be amended as follows:

a. all cyanazine labels require the use of protective gloves when mixing or loading cyanazine or when adjusting, repairing, or cleaning equipment;

b. all cyanazine labels require that protective gloves be washed with soap and water after use and before being removed from the hands;

c. all cyanazine labels require the use of closed loading systems in connection with aerial use and chemigation (product formulations which cannot be used in a closed loading system must prohibit aerial use and chemigation);

d. all cyanazine labels require the use of a chemical resistant apron when mixing and/or loading;

e. all cyanazine labels are required to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water; and

f. all cyanazine labels are required to include the following precaution concerning the washing of contaminated clothing:

> Cyanazine contaminated clothing should be laundered separately from household laundry to prevent cross-contamination of other laundry. Heavily contaminated or drenched clothing and protective equipment must be discarded or destroyed in accordance with State and local regulations.

F. Procedural Matters

These proposed decisions are being submitted to the United States Department of Agriculture and the Science Advisory Panel for review, as required by FIFRA, sections 6 and 24, respectively. Furthermore, public comments are solicited on these proposed label requirements and any other aspects of the Agency's proposed regulatory decisions on cyanazine.

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ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

[OPP-30000/46A; FRL]

NOTICE OF PRELIMINARY DETERMINATION TO CANCEL REGISTRATIONS OF CYANAZINE PRODUCTS UNLESS THE TERMS AND CONDITIONS OF THE REGISTRATION ARE MODIFIED; NOTICE OF AVAILABILITY OF TECHNICAL SUPPORT DOCUMENT AND DRAFT NOTICE OF INTENT TO CANCEL

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of Preliminary Determination.

SUMMARY: This Notice sets forth EPA's preliminary determination regarding the continued registration of pesticide products containing cyanazine and discusses the Agency's assessment of the risks and benefits associated with the pesticidal uses of cyanazine. On April 10, 1985, EPA issued a Notice of Initiation of Special Review of Registrations of Products Containing Cyanazine. This Notice announces the Agency's preliminary determination to allow continued use of registered cyanazine pesticide products only if registrants modify certain terms and conditions of registration as noted herein. In addition, this Notice announces the availability of the Cyanazine Technical Support document and a draft Notice of Intent to Cancel. The Technical Support Document and accompanying science reviews comprise the technical documents in support of this preliminary determination.

DATE: Written comments must be received on or before (insert date 60 days after date of publication in the FEDERAL REGISTER).

ADDRESS: Submit three copies of written comments, bearing the document control number "OPP-30000/46A, by mail to:

Information Services Section,
Program Management and Support Division (TS-757C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St., SW.,
Washington, D.C. 20460.

In person bring comments to:
Rm. 236, Crystal Mall Building #2,
1921 Jefferson Davis Highway,
Arlington, VA.

Information submitted in any comment concerning this Notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR Part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public docket. Information not marked CBI may be disclosed publicly by EPA without prior notice to the submitter. The cyanazine public docket, which contains all non-CBI written comments, and the corresponding index, will be available for public inspection in Rm. 236 at the Virginia address given above, from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

FOR FURTHER INFORMATION CONTACT: For general information, contact by mail:

Joanna Dizikes,
Registration Division (TS-767C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St., SW.,
Washington, D.C. 20460.
Office location and telephone number:
Rm. 1006, Crystal Mall Building #2,
1921 Jefferson Davis Highway,
Arlington, VA 22202,
(703-557-5096).

For a copy of the Technical Support Document, to request information concerning the Special Review public docket, or to request indices to the Special Review public docket, contact Frances Mann (703-557-2805). It is suggested that such material be requested no later than [insert date 30 days after date of publication in FEDERAL REGISTER] to allow sufficient time for the requestor to receive the material before the close of the comment period.

SUPPLEMENTARY INFORMATION: This Notice is organized in the following units. Unit I provides the background on cyanazine and the initiation of the Special Review. Unit II provides the legal background. Unit III provides a summary of the risk and benefit determinations and proposed regulatory actions. Unit IV sets forth procedural matters. Unit V discusses the opportunity for public comment. Unit VI includes information on the public docket.

I. BACKGROUND

Cyanazine is the accepted, common name for 2-(4-chloro-6-ethylamino-s-triazine-2-ylamino)-2 methyl propionitrile, and its trade name is Bladex®. Pesticide products containing cyanazine have been registered since 1971; there have been three registrants of cyanazine products in the United States: Shell Chemical Company; R. F. Lindsey & Sons; and Setre Chemical Company. With the exception of Shell's registered, cyanazine products, all other registered, cyanazine products have been canceled voluntarily.

Cyanazine is a pre- or postemergent herbicide, registered for use to control annual grasses and broadleaf weeds in corn, cotton, grain sorghum (milo), and fallow cropland which may subsequently be planted to wheat. Approximately 95% of the total domestic usage is on corn. Cotton (3%) is the second most common use, and grain sorghum (1%) and wheat fallow (<1%) are the other use sites.

On January 3, 1985, EPA issued a Registration Standard for pesticide products containing cyanazine. In addition to requiring certain data be submitted, the Standard announced the Agency's position on continued registration including certain labeling changes which should be made. These changes included, among others, making the pesticide a restricted use pesticide and the addition of a statement that it causes birth defects in laboratory animals.

On April 10, 1985, EPA issued a Notice of Special Review (also called Position Document 1 or "PD 1") for pesticide products containing cyanazine (50 FR 14151). EPA initiated the Special Review on pesticide products containing cyanazine following the determination that cyanazine met or exceeded the risk criterion in 40 CFR 162.11(a)(3)(ii)(B), which were in effect at that time. The new, revised risk criterion for chronic or delayed toxic effects, issued in the November 27, 1985 FEDERAL REGISTER, incorporates oncogenicity, mutagenicity, and teratogenic effects, as well as other chronic or delayed toxic effects. [See 40 CFR 154.7(a)(2).] The risks of cyanazine use, as described in Part III of this Notice, exceed the new criteria as well.

The Special Review was based on teratology studies showing that cyanazine was teratogenic and fetotoxic in laboratory animals. Specifically, a study with Fisher 344 rats showed orally administered cyanazine to be teratogenic at 25 mg/kg (No-Observed-Effect Level (NOEL)= 10 mg/kg). The teratogenic effects were anophthalmia (no eyes), microphthalmia (small eyes), and diaphragmatic hernia. Cyanazine also was shown to cause fetotoxic effects when fed to New Zealand rabbits at 2 mg/kg (low litter weights), with dilated brain ventricles, anophthalmia, and microphthalmia at 4 mg/kg. The NOEL for this study was 1 mg/kg. Additionally, the Agency determined that the teratogenic potential of cyanazine posed a significant risk through dermal exposure to mixers/loaders and applicators who use pesticide products containing cyanazine.

The basis of EPA's decision to initiate the Special Review on cyanazine is further detailed in a document entitled "Guidance for the Reregistration of Pesticide Products Containing Cyanazine" (Guidance Document) which was issued in December 1984. In the PD 1, which was issued in April 1985, EPA solicited comments on the risks and benefits associated with all uses of cyanazine.

Based on information received in the public comments, as well as on additional data and analyses (including a dermal absorption study and two dermal teratology studies) which have become available since initiation of the Special Review, EPA has made a preliminary determination to cancel the registration of products containing cyanazine unless certain modifications of the terms and conditions of registration are made by registrants. EPA's position and a summary of the rationale underlying that position is set forth in this Notice. The basis for EPA's actions are explained more fully in the cyanazine Technical Support Document, copies of which are available upon request from the contact person identified earlier.

In accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA is sending a copy of this Notice, the Technical Support Document, and the draft Notice of Intent to Cancel to the Secretary of Agriculture and the Scientific Advisory Panel for the required 30-day review. EPA is also providing a 60-day public comment period on these documents. After reviewing any comments received within the applicable time limits, EPA will determine what final regulatory actions are appropriate.

II. LEGAL BACKGROUND

A. THE STATUTE

A pesticide product may be sold or distributed in the United States only if it is registered or exempt from registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended (7 U.S.C. 136 et seq.). Before a product can be registered it must be shown that it can be used without "unreasonable adverse effects on the environment" (FIFRA section 3(c)(5)), that is, without causing "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of the pesticide" (FIFRA section 2(bb)). The burden of proving that a pesticide meets this standard for registration is, at all times, on the proponent of initial or continued registration. If at any time the Agency determines that a pesticide no longer meets this standard for registration, then the Administrator may cancel this registration under section 6 of FIFRA.

B. THE SPECIAL REVIEW PROCESS

The Special Review process, formerly called the Rebuttable Presumption Against Registration (RPAR), is a mechanism by which the Agency collects information on the risks and benefits associated with the uses of pesticides to determine whether any use causes unreasonable adverse effects to human health or the environment. The Special Review process is currently governed by 40 CFR Part 154.

Through the Special Review process the Agency (1) announces and describes the Agency's finding that use of a pesticide meets one or more of the risk criteria; (2) establishes a public docket; (3) solicits comments from the public and, under certain circumstances, from the Secretary of Agriculture and the Scientific Advisory Panel regarding the Agency's analysis and proposed regulatory decisions; (4) reviews and responds to all significant comments submitted in a timely manner; and (5) makes a final regulatory decision based on a balancing of risks and benefits associated with a pesticide's use.

Issuance of this Notice means that potential adverse effects and benefits associated with the use of pesticide products containing cyanazine have been assessed and that the Agency has preliminarily determined that, unless the terms and conditions of registration are modified as proposed in this Notice, the risks from exposure to cyanazine outweigh the benefits of its use.

As noted in the section of this Notice entitled FOR FURTHER INFORMATION CONTACT, a document entitled "Cyanazine Technical Support Document" (Technical Support Document) has been developed and is available to the public. The Technical

Support Document provides a detailed explanation of the basis for EPA's preliminary decision and also contains references, background information, and other information pertinent to the registration of pesticide products containing cyanazine.

In addition, copies of a draft Notice of Intent to Cancel Registrations of Cyanazine Products are also available from the contact person listed above. Preparation of the draft Notice of Intent to Cancel is required by 40 CFR §154.31 (b)(1). This draft Notice must be forwarded to the Scientific Advisory Panel and the Secretary of Agriculture to permit their review of the Agency's action. The draft Notice of Intent to Cancel, together with the Cyanazine Technical Support Document and the other notice and analyses prepared pursuant to 40 CFR §154.31 are being sent to all registrants and applicants for registration of cyanazine products. The draft Notice of Intent to Cancel contains the provisions regarding disposition of existing stocks, compliance by intrastate producers, and procedures for requesting a cancellation or denial hearing.

III. SUMMARY OF THE RISK AND BENEFIT DETERMINATIONS AND PROPOSED REGULATORY ACTIONS

A. DETERMINATIONS ON RISKS

The margins of safety presented in the Registration Standard and Notice of Initiation of Special Review (PD 1), with respect to dermal exposure, were based on a NOEL from an oral developmental toxicity study. A dermal developmental toxicity study was not available at the time the Special

Review was initiated. A dermal developmental toxicity study has since been submitted and was used to determine risks to mixers/loaders and applicators from dermal exposure.

1. TERATOGENICITY

As noted earlier, after the Special Review was initiated on cyanazine, the Agency received two dermal teratology studies. The first developmental toxicity study was in New Zealand rabbits using the Bladex® 4L formulation and resulted in maternal toxicity at all dose levels, including the lowest dose used; therefore, a no-observed-effect-level (NOEL) for maternal toxicity could not be established for this study, and the lowest-effect-level (LEL) was established at the lowest dose used, 0.2 ml/kg. Because the study did not permit establishment of a NOEL and because the number of litters per test group was not sufficient, the study was not used for a quantitative risk assessment.

The second dermal teratology study submitted was a repeat study of the study discussed in the prior paragraph. In this repeat study, a maternal NOEL was demonstrated at < 96 mg/kg (lowest dose tested), and the developmental toxicity NOEL was established at 573 mg/kg.

As demonstrated by these studies, the dermal route of exposure did not lead to frank teratogenic effects, although developmental toxicity was demonstrated. The reduced effects seen via the dermal route are probably related to the low observed rate of dermal absorption; only 2% of the applied dose of Bladex® was absorbed in a dermal absorption study conducted on rats, which also was submitted following initiation of the Special Review.

Additionally, following initiation of the Special Review, the Agency received two worker exposure studies conducted with cyanazine. These studies were used to estimate the dermal exposure to individuals when mixing and loading cyanazine while wearing gloves and using a closed tractor cab and dermal exposure when utilizing gloves and an open cab tractor. Surrogate exposure studies were used to estimate the dermal exposure during mixing/loading operations for aerial application and chemigation when no protection is used, only protective gloves are used, and when both protective gloves and closed loading systems are used.

Based on the NOEL (573 mg/kg) from the dermal developmental toxicity study in rabbits and the exposure estimates determined above, the MOS's were developed using the following formula:

$$\text{Margin-of-safety (MOS)} = \frac{\text{Dermal Developmental Toxicity NOEL}}{\text{Exposure Level}}$$

The Agency generally considers a MOS above 100 to be acceptable. The resulting MOS's for the various uses of cyanazine are given below:

a. Ground Boom Application

i. Corn

The MOS's given in Table 1 represent the risks to applicators, mixers, and loaders. (The risk assessments for ground boom use assume that the mixer/loader and the applicator are the same person.)

While, the MOS's vary depending on use rate and acreage treated, as shown in Table 1, the MOS's are adequate for all application rates to corn when protective gloves are worn during mixing and loading operations and when adjusting, repairing, or cleaning equipment.

ii. Cotton, Milo, and Wheat Fallow

The usage of cyanazine on cotton, milo and wheat fallow amounts to less than 5% of all cyanazine use. As noted in Table 1, the MOS's are adequate for all application rates to these crops when protective gloves are worn during mixing and loading operations and when adjusting, repairing, or cleaning equipment.

Table 1

MARGINS OF SAFETY FOR GROUND BOOM APPLICATION*

	Corn	Cotton	Wheat Fallow	Milo
Applicator**				
No protection	7	21	11	21
Gloves	670	1980	990	1980
Gloves/closed cab	4240	12730	6370	12730

* The MOS's in this table are for the highest use rates.

** Assumes that mixer/loader and applicator are the same person.

b. Aerial Application

Aerial application to corn is minimal. There are no data showing that cyanazine is being aerially applied to cotton, wheat fallow, or sorghum.

As shown in Table 2, the MOS's for mixer/loaders during aerial use are not acceptable unless protective gloves are worn during mixing and loading operations and when adjusting, repairing, or cleaning equipment and a closed loading system is used.

Product formulations which cannot be used in a closed loading system would have to prohibit aerial application.

Table 2

MARGINS-OF-SAFETY FOR AERIAL APPLICATION*

	Grain Sorghum	Corn	Wheat Fallow
Applicator (Pilot)	320	170	250
Mixer/Loader			
No Protection (open pour)	5	2	2
Gloves (open pour)	24	11	12
Gloves/Closed System	1000	440	520

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* The MOS's in this table are for the highest use rates.

c. Chemigation

Corn is the only crop for which chemigation is listed on the label as an application method. As shown in Table 3, the MOS's for chemigation are not acceptable unless both protective gloves are worn during mixing and loading operations and when adjusting, repairing, or cleaning equipment and a closed loading system is used. Product formulations which cannot be used in a closed loading system would have to prohibit use of chemigation.

Table 3

MARGINS OF SAFETY FOR CHEMIGATION*

	Corn
Applicator	
No Protection (open pour)	13
Gloves (open pour)	59
Gloves/Closed System	2490

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* The MOS's in this table are for the highest use rates.

79

d. Spray Drift and Secondary Exposure

Surrogate exposure studies were used to estimate exposure to cyanazine through spray drift. Based on these exposure estimates the MOS for a population exposed to cyanazine by spray drift would be over 1000. Secondary exposure may also occur when contaminated clothes are brought home. Although data are not available to quantify such exposure, data do show that cross-contamination does occur when contaminated clothes are washed with household laundry. The Agency, therefore, believes that cyanazine contaminated clothes should be washed separately from household laundry to prevent cross-contamination of other laundry.

e. Chemical Resistant Aprons

While the risk of dermal exposure to the body from leaning against tanks during mixing or loading operations, a common practice, and accidental spills cannot be quantified, they may be significant in light of the teratogenic effects of cyanazine. The Agency, therefore, believes that a chemical resistant apron should be worn when mixing or loading cyanazine.

f. Washing of Protective Gloves

Because hands receive the largest percentage of the dermal exposure during mixing/loading, it is assumed that the protective gloves will be contaminated on the outside with a large percentage of the cyanazine being handled. Therefore, the Agency believes that language should be added to all cyanazine labels which states that protective gloves must be washed with soap and water after use and before being removed from the hands.

g. Restricted Use

All cyanazine products are already required to be classified for restricted use. Furthermore, Agency policy states that when a pesticide is classified for restricted use the reason for that classification must be printed in the "Restricted Use" statement which appears on the label. Therefore, all cyanazine labels are required to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water.

B. DETERMINATION OF BENEFITS

1. GROUND BOOM APPLICATION

The largest use of cyanazine is on corn, accounting for about 95 percent of its total annual usage. Approximately 4.6 million acres (14 to 16% of the total U.S. corn acreage) of corn were treated in 1982 with cyanazine as the sole active ingredient. Cyanazine is applied to corn as a preemergence or postemergence broadcast application by ground equipment in the spring. Growers select cyanazine over currently available herbicides for the following reasons: 1) it has a wide annual broadleaf and grass weed control spectrum; 2) it can be tank-mixed with a number of herbicides to broaden its weed control spectrum; 3) it has relatively short persistence in the soil; and 4) it has no rotational crop restrictions.

There are several alternatives to cyanazine, and the Agency assumes that there would be no significant increase in production costs if they are used. A limited number are registered which control as wide a spectrum of weeds as cyanazine. Atrazine is the major alternative to cyanazine for pre- or postemergent control. Also, atrazine is the most widely used herbicide on corn; however, residues may carry over in the soil to the next crop and limit the growers' options for rotational crops.

Cyanazine is reported to be better than alachlor for the control of grasses and is often recommended when grassy weeds are a concern. Atrazine does not adequately control foxtail and other annual grasses at lower rates or under low rainfall conditions as well as does cyanazine. Other herbicides which compete with cyanazine are simazine, a tank mix of butylate and atrazine, and package mixes of metolachlor and atrazine and atrazine and propachlor. These tank mixes have a smaller weed control spectrum, and those mixed with atrazine still produce a carryover effect.

Cyanazine rates above 2.5 lbs ai per acre are used on high organic matter soils (above 3% organic matter), on soils with a pH greater than 7.0, and on wet/cool soils, because atrazine cannot be used at effective rates on these soils without excessive phytotoxicity to rotational crops. In the following areas, only cyanazine is available as a preemergence control for the cyanazine grass/broadleaf weed complex: North Central Iowa; South East Minnesota; parts of Wisconsin, Michigan, New York, and Pennsylvania; and the Blackland soils area of Texas. Generally, one pound of triazine is needed for each percent of organic matter for effective weed control.

Atrazine is the most likely chemical alternative to cyanazine for weed control. However, cyanazine has short soil persistence when compared to atrazine. Thus, phytotoxicity may result from atrazine carry-over when atrazine is used on certain soil types.

Only 1 percent of the wheat fallow acreage grown in the United States is treated with cyanazine. Mechanical tillage is still the most common form of weed control and is used on 50 to 90 percent of the total fallow wheat acreage.

Cyanazine is valuable in most wheat fallow programs involving the use of chemicals because of its broad spectrum weed control and short term soil residual activity. Atrazine is an alternative, soil active herbicide that, unlike cyanazine, is highly persistent. Under those conditions that favor herbicide persistence, atrazine residues are often still available in the soil at the fall planting of the wheat, resulting in crop phytotoxicity. Atrazine can sometimes be applied at reduced rates to minimize the carry-over problem, but weed control consequently becomes less reliable.

The weed control spectra of cyanazine and atrazine are generally considered to be similar. Cyanazine does not provide good control of pigweed but generally provides better control of grasses, especially fall panicum and crabgrasses.

In cotton, cyanazine may be applied preemergent, directed early postemergent or as a layby (late) postemergent directed treatment. It can be tank mixed with norflurazon as a preemergent treatment or with MSMA as a postemergence directed spray. Both cyanazine and the tank mix with norflurazon are recommended as the best treatment to control spotted spurge. Possible alternatives to cyanazine use in cotton would be prometryn, fluometuron, and diuron; however, cyanazine is registered for control of more weeds than any of the other three herbicides. Diuron has more rotational crop restrictions than does cyanazine. Approximately 84 percent of the cyanazine used on cotton is reported to be applied as a directed post-emergence treatment. The remaining 16 percent is applied as preemergent treatments.

Cyanazine may be applied to grain sorghum as a preemergent application but only when tank mixed with propachlor or with propazine. These tank mixes cannot be used on sand, sandy loam, loamy sand, and peat or muck soils. Also, these tank mixes have several geographical restrictions because of possible crop injury under stress conditions. Potential alternatives to cyanazine include propachlor and atrazine as a tank or package mix, and the package mix of metolachlor and atrazine. These alternatives except for propachlor also carry crop rotational or regional restrictions. The cyanazine tank mixes appear to control more broadleaf weeds than the alternatives. Generally, the tank mix of cyanazine and propazine is believed to give better control of broadleaf weeds than the cyanazine and propachlor tank mix. However, cyanazine tank mixes are generally less effective on cocklebur and morningglory.

2, AERIAL APPLICATION

Cyanazine is most frequently applied for preemergent weed control in corn. Preemergent chemicals are rarely applied aerially since it is relatively easy for a grower to apply these types of herbicides during other agricultural operations. Available data indicate that approximately

70,000 acres of corn are treated aerially with cyanazine. There are no data showing that cyanazine is being applied aerially to cotton, wheat fallow or sorghum.

3. CHEMIGATION

No significant usage of cyanazine through chemigation has been reported.

C. RISK/BENEFIT ANALYSIS

The Agency has determined that, with current label restrictions, the risks posed to applicators, mixers and loaders outweigh the benefits from use of cyanazine to corn, cotton, wheat fallow and sorghum.

There are several registered, alternative pesticides for ground boom use on sorghum, cotton, and wheat fallow, as well as mechanical tillage for weed control in wheat fallow. There are several, registered alternative pesticides for use on corn at the lower use rates (<2.5 lbs a.i. per acre), which the Agency assumes can be used with no significant increase in production costs. For rates above 2.5 lbs a.i. per acre, atrazine is the only available alternative for ground boom use on corn to control some weeds, and under certain conditions it cannot be used.

The Agency believes the risks posed from ground boom use of cyanazine can be lowered to acceptable margins with the use of protective gloves during mixing and loading and adjusting, repairing or cleaning equipment and the use of chemical resistant aprons during mixing and loading operations.

The costs involved to comply with these restrictions are minimal in comparison to the risks involved. Such compliance will allow continued availability of cyanazine for use through ground boom application and preserve the benefits of its use.

The Agency has determined that, under current restrictions, the risks posed to applicators, mixers and loaders outweigh the benefits from use of cyanazine through aerial application and chemigation.

Cyanazine is rarely applied aerially since it is relatively easy for a grower to apply it via ground boom during other agricultural operations. There is an insignificant acreage of corn treated aerially (approximately 70,000 acres). There are no data showing that cyanazine is being applied aerially to cotton, wheat fallow or sorghum. No significant usage of cyanazine through chemigation has been reported.

The Agency believes the risks posed from aerial and chemigation uses of cyanazine can be lowered to acceptable margins with the use of: 1) protective gloves during mixing and loading and adjusting, repairing or cleaning equipment; 2) the use of chemical resistant aprons during mixing and loading operations; and 3) the use of a closed loading system. Product formulations which cannot be used in a closed loading system would have to prohibit aerial use and chemigation. The costs involved to comply with these restrictions are minimal in comparison to the risks involved. Such compliance will allow continued availability of cyanazine for use through aerial application and chemigation and preserve the benefits of its use.

The Agency has determined that secondary exposure may also occur when contaminated clothes are brought home. Available data show that cross-contamination does occur when contaminated clothes are washed with household laundry. Although data are not available to quantify such exposure, the Agency believes it prudent that a precautionary statement be added to the label concerning the need to wash cyanazine contaminated clothes separately from other household laundry. There are minimal costs involved to the user from such a precaution.

Because hands receive the largest percentage of the dermal exposure during mixing/loading, it is assumed that the protective gloves will be contaminated on the outside with a large percentage of the cyanazine being handled. Therefore, the Agency believes that language should be added to all cyanazine labels which states that protective gloves must be washed with soap and water after use and before being removed from the hands.

All cyanazine products are already required to be classified for restricted use. Furthermore, Agency policy states that when a pesticide is classified for restricted use the reason for that classification must be printed in the

"Restricted Use" statement which appears on the label. Therefore, all cyanazine labels are required to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water.

D. PROPOSED REGULATORY ACTIONS

The proposed regulatory actions specified herein are based on the assumption that registered products are in compliance with Agency regulatory positions announced in the cyanazine registration standard.

1. GROUND BOOM APPLICATION

It is proposed that cyanazine labels require the use of protective gloves when mixing or loading, or when adjusting, repairing, or cleaning equipment. Furthermore, because dermal exposure to the body results commonly from leaning against tanks during mixing or loading operations and because accidental spills may occur, it is further proposed that cyanazine labels require the use of a chemical resistant apron when mixing or loading cyanazine for ground boom use.

2. AERIAL APPLICATION AND CHEMIGATION

It is proposed that cyanazine labels require both the use of protective gloves (i.e. when mixing or loading, or when adjusting, repairing or cleaning equipment) and the use of a closed loading system, when applying cyanazine through aerial or chemigation methods. Product formulations which cannot be used in a closed loading system would have to prohibit aerial use and chemigation. In addition, it is further proposed that cyanazine labels require the use of a chemical resistant apron when mixing and loading cyanazine to protect against accidental spills and closed loading system failures. Closed loading systems may break down and hoses may rupture, sending a hard spray of the pesticide onto the mixer or loader. Also, as during ground boom operations, dermal exposure to the body from leaning against tanks during mixing and loading is also very common during aerial use and chemigation.

3. LAUNDERING OF CONTAMINATED CLOTHES

It is proposed that the cyanazine labels require the following precaution concerning laundering of contaminated clothing:

> Cyanazine contaminated clothes should be laundered separately from household laundry to prevent cross contamination of other laundry. Heavily contaminated or drenched clothing and protective equipment must be discarded or destroyed in accordance with State and local regulations.

4. WASHING OF PROTECTIVE GLOVES

It is proposed that cyanazine labels require the following precaution concerning the washing of protective gloves:

> Protective gloves must be washed with soap and water after use and before removing from the hands.

5. RESTRICTED USE

All cyanazine products have been required to be classified for restricted use. Furthermore, all cyanazine labels are required to add to their "Restricted Use" statement that cyanazine products have been classified for restricted use because cyanazine has caused birth defects in laboratory animals and has been found in ground water.

IV. PROCEDURAL MATTERS

A. REFERRAL TO THE SECRETARY OF AGRICULTURE AND THE SCIENTIFIC ADVISORY PANEL

As required by FIFRA sections 6(b) and 25(d), and 40 CFR 154.31(b), EPA will transmit copies of this Notice, a draft Notice of Intent to Cancel and the support documents, to the Secretary of Agriculture and the Scientific Advisory Panel for comment. If either the Secretary or the Panel comments in writing on EPA's proposed action within 30 days of receipt of the draft Notice and support documents, the Agency must publish any comments received from the Secretary or the Panel, and EPA's responses, in the Notice of Final Determination.

B. INTRASTATE PRODUCTS

Pursuant to 40 CFR 162.17, EPA hereby notifies producers of all cyanazine products registered solely for intrastate sale and distribution that they are required to submit a complete application for Federal registration. These applications must be submitted within 60 days of the date on which this Notice is published in the FEDERAL REGISTER or the date on which the intrastate producer receives a copy of this Notice, whichever is later. If an intrastate producer fails to submit a timely application, EPA will consider his Notice of Intent to Apply as an application for Federal registration for purposes of the review described below.

EPA will review all applications submitted. If EPA decides, in light of comments received in response to this Notice, to issue a final notice allowing continued use of cyanazine products under certain circumstances, EPA will notify intrastate producers of that decision and allow them at least 30 days in which to make changes that would allow EPA to approve the application for Federal registration. If the application has not been corrected in the prescribed manner within the period allowed, the application may be denied. On the other hand, if EPA issues a final notice cancelling the registrations of cyanazine products, that notice will also include a final Notice of Denial for all applications for Federal registration of intrastate pesticide products containing cyanazine for uses subject to that Notice.

Under FIFRA section 3(c)(6), the issuance of a denial notice entitles an applicant, or other interested person with the concurrence of the applicant, to request an adjudicatory hearing to challenge the denial decision. The procedures for requesting a hearing and the consequences of not filing a request are discussed below in Unit IV.C.1.

C. PROCEDURES FOR RESPONDING TO NOTICE OF FINAL DETERMINATION

1. HEARING REQUEST

Registrants, applicants, and other interested parties who would be adversely affected by any decision to cancel or deny applications for the registration of cyanazine products would be entitled to request a hearing in which to contest EPA's final decision to cancel registrations and deny applications for failure to comply with the modifications to registration listed in Unit III.D of this notice. Under FIFRA, such persons must submit their requests for a hearing within 30 days either of receipt of the final Notice of Intent to Cancel or Notice of Denial or of its publication in the FEDERAL REGISTER, whichever is later. As EPA will explain in detail in any final Notice of Intent to Cancel or Notice of Denial, a hearing request must contain information concerning the basis of the request. If a timely, properly formulated hearing request is submitted and a hearing is initiated, the product registrations which are the subject of the request will remain in effect during the cancellation hearing.

Similarly, applications for registration with respect to which valid and timely hearing requests have been filed remain pending unless and until they are denied or granted by order of the Administrator at the conclusion of the hearing.

If a proper and timely hearing request is not submitted for a product, registration of that product would be cancelled, or in the case of intrastate products, the application would be finally denied by operation of law 30 days after the final Notice was issued. A final cancellation or denial would have the effect of prohibiting further sale and distribution, except as specified in any existing stocks provision included in the final notice.

2. AMENDMENT OF REGISTRATION OR APPLICATION

Registrants who would be affected by any final decision to cancel the registrations of cyanazine products unless the terms and conditions of the registrations are modified may avoid cancellation, without requesting a hearing, by filing an application for an amended registration that contains the label modifications detailed in the Notice of Final Determination. This application must be filed within 30 days of receipt of the final notice, or within 30 days of publication of the final notice, whichever occurs later. Similarly, applicants for a registration that would be subject to the final notice would have to file an amended application for registration within the applicable 30-day period to avoid denial of the application.

It should be noted that registrants (and applicants) are not required to request a hearing or to amend their registrations (or applications) at this time in order to be allowed to to continue to sell and distribute their products within this period.

V. PUBLIC COMMENT OPPORTUNITY

The Agency is providing a 60-day period to comment on this Notice and on the cyanazine Technical Support Document. The Agency is particularly soliciting comments on the issues discussed in Unit III above. Comments must be submitted by (insert date 60 days after date of publication in the FEDERAL REGISTER). All comments and information should be submitted in triplicate to the address given in this Notice under ADDRESS, to facilitate the work of EPA and others interested in inspecting them. The comments and information should bear the identifying notation OPP-30000/46A. All comments, information, and analyses which come to the attention of EPA may serve as a basis for final determination of regulatory action during the Special Review.

During the comment period, interested members of the public or registrants may request a meeting to discuss factual information available to the Agency, to present any factual information, to respond to presentations by other persons, or to discuss what regulatory actions should be taken regarding cyanazine. Persons interested in arranging such meetings should contact the Review Manager listed in this Notice under FOR FURTHER INFORMATION CONTACT.

VI. PUBLIC DOCKET

Pursuant to 40 CFR 154.15, the Agency has established a public docket (OPP-30000/40A) for the Cyanazine Special Review. This public docket includes (1) this Notice; (2) any other notices pertinent to the cyanazine Special Review; (3) non-CBI documents and copies of written comments or other materials submitted to the Agency in response to this Notice, and any other Notice, regarding cyanazine submitted at any time during the Special Review process by any person outside government; (4) a transcript of any public meeting held by the Agency for the purpose of gathering information on cyanazine; (5) memoranda describing each meeting held during the Special Review process between Agency personnel and any person outside government pertaining to cyanazine; and (6) a current index of materials in the cyanazine public docket.

On a monthly basis, the Agency will distribute a compendium of indices for newly received comments and documents that have been placed in the public docket for this Special Review. This compendium will be distributed by mail to those members of the public who have specifically requested such material for this Special Review, pursuant to 40 CFR 154.15(f)(3).

Dated: DEC 29 1986

Assistant Administrator,
Office of Pesticides and
Toxic Substances